ON NEUROMA
AND
NEURO-FIBROMATOSIS

ALEXIS THOMSON

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AND

NEURO-FIBROMATOSIS

BY

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PREFACE

THE author's interest in the subject of Neuroma and allied conditions was excited by the opportunities which were afforded him of observing a remarkable series of cases (fifteen in number) in the wards of the Edinburgh Royal Infirmary during the last six years.

So far as relates to the True Neuroma, the author has been entirely dependent upon the observations of others, while unfortunately he has been unable to make any special study of tumours of the optic nerve.

The author desires to express his great indebtedness to Professor Annandale for invaluable opportunities of clinical observation, and for almost the entire pathological material on which the present dissertation is founded. He is also indebted to Professor T. R. Fraser, Mr A. G. Miller, Dr Alexander Bruce, Dr Welsh, Dr Lundie, Mr Hodsdon, Mr Dowden, Dr Murray Leslie, Dr Thomson of Dumfries, Dr Graham, and Dr John Balfour of Portobello, for notes of cases and for pathological material.

Mr Richard Muir, of the Pathological Department of the University, is responsible for the preparation of the material for microscopical examination, and Mr J. Hume Patterson, of the Royal College of Physicians Laboratory, for the majority of the microphotographs.

The great variety of the morbid conditions referred to has induced the author to illustrate these wherever possible. Since, however, the material at his disposal does not cover the entire scope of the subject, he has thought it advisable to introduce a certain number of illustrations derived from other sources.

32 RUTLAND SQUARE,
EDINBURGH.

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CHAPTER I

INTRODUCTORY

Tumours of nerves have been the subject of observation from the earliest times. The fascination exerted by the characteristic clinical features, and by the capacity of demonstrating the very obvious relationship between these and the tumour giving rise to them, has resulted in the recording of innumerable cases in a permanent form. Medical literature so abounds with references to the subject that a complete bibliographical index would require a volume to itself. The author does not pretend to have exhausted the resources of the libraries of the two Royal Colleges of Edinburgh, but he is indebted to them for obtaining access to the more important contributions to the subject, from the beginning of the present century. A paper by William Wood,[1] a Fellow of the Royal College of Surgeons, published in the Transactions of the Medico-Chirurgical Society of Edinburgh in 1829, is the earliest to which he has obtained access. According to Wood, the term "neuroma" was introduced by Odier[2] of Geneva in 1803, to designate "tumours formed by diseased enlargements of the nerves." Wood gives a classical description of the anatomical and clinical features of the disease, and records no less than twenty-four cases of neuroma, which he had collected from various sources. Wood refers also to the occurrence of multiple neuromata, and to the changes which follow upon the division of nerves. In discussing the origin of neuromata, it is interesting to find that he believed them to originate from the connective tissue

[1] William Wood. "Observations on Neuroma," Edin. Med. Chir. Trans., Vol. III. 1829.

[2] Louis Odier. "Manuel de Médecine pratique." Genève, 1811.

sheaths of the nerve, and not from the nerve tissue itself. In treatment, he remarks on the ineffieaey of medieines and of external applieations, and reeommends removal of the tumour by operation. Eight cases are quoted in whieh the tumour was sueeessfully removed : one from Cheselden's "Anatomy of the Human Body," published in 1773 ; one from the "Encyelopédie Methodique de Chirurgie" (Paris, 1792), in whieh amputation was performed for what was undoubtedly a plexiform neuro-fibroma of the median nerve in the forearm ; and a third from a paper by Sir Everard Home,[1] relating a case in which he assisted John Hunter to excise a tumour of the museulo-cutaneous nerve in the upper arm. Another ease of historieal interest is that reeorded by Sir Charles Bell,[2] in whieh he removed a tumour from the internal popliteal nerve ; this speeimen is preserved in the Museum of the Royal College of Surgeons of Edinburgh. Among other early papers on neuroma, mention should be made of those by Daniel Pring of London in 1815, by Aronsohn of Strasburg in 1822, by Deseot of Paris in 1825, and by Knoblaneh in 1843. Next in chronologieal order, appeared the well-known work[3] of R. W. Smith of Dublin in 1849. Smith classified neuromata into those whieh are of spontaneous origin, and those whieh result from injuries of nerves, ineluding among the latter, those forming at the eut ends of nerves. His deseription of the general eharaeters of neuromata is elassical, and has been universally recognised as sueh, while the large plates which illustrate his work may be deseribed as masterpieees of engraving. Smith was able to give an exhaustive aeeount of the disease known as "Multiple Neuromata," based upon the post-mortem examination of two of the most remarkable eases of that disease on reeord. While adopting the

[1] Transaetions of a Society for the Improvement of Medical and Surgieal Knowledge. London, 1800.

[2] "A System of Operative Surgery." London, 1814.

[3] R. W. Smith. "A Treatise on the Pathology, Diagnosis and Treatment of Neuroma." Dublin, 1849.

term "neuroma" as applicable to all tumours of nerves, he did not regard them as composed of nerve tissue; he agrees with Wood in ascribing their origin to an overgrowth of the connective tissue sheaths of the nerves, and apparently takes it for granted that a tumour composed of nerve tissue does not exist. It is a remarkable fact that neither Smith nor any of his predecessors, describe the occurrence of sarcomata of nerves. As regards treatment, Smith disapproved of any operative procedure in which an attempt was made to remove the tumour by dissection from the nerve bundles which surrounded it, because the patient usually succumbed to the "inflammation of the nerve" which frequently supervened. He advised amputation, or removal of the affected portion of nerve along with the tumour. He quotes Velpeau,[1] and agrees with him in the observation that recovery of function may be confidently anticipated after resection of even considerable portions of the main nerve trunks of the limbs, an observation which has since been repeatedly confirmed. For Smith and his predecessors and contemporaries, the mere anatomical connection of a tumour with a nerve was regarded as sufficient to warrant its being regarded as a neuroma, whatever its structure might be; hence, from the outset, the term "neuroma" has been employed to include tumours of very various kinds, and a number of diseased conditions which are not tumours at all. At the same time, the term has crept into such general use, that it would be unwise to alter its significance; it is a convenient term, and employed in the clinical sense, it indicates the most important feature of any particular tumour, viz., its seat in a nerve, irrespective altogether of its structure. Virchow's lectures on the "Krankhaften Geschwülste,"[2] published in 1863, placed the pathology of neuromata on a new basis. Although the histology of nerve tissue was

[1] Velpeau. "Leçons orales de Clinique Chirurgicale." Paris. Vol. III.
[2] Rudolf Virchow. "Die Krankhaften Geschwülste." Berlin, 1863. Vol. III.

then in its infancy, he endeavoured to classify neuromata on a structural, instead of a clinical basis, dividing them, in the first instance, into the true and the false; the former (the neuroma verum) being defined as a tumour which is mainly composed of new nerve tissue, or one into the composition of which newly-formed nerve tissue enters as an essential constituent. The latter (pseudo-neuroma) is composed of connective tissue derived from the sheaths of the nerve. He further differentiated the true neuromata into three groups, one containing newly-formed nerve cells (neuroma ganglio-cellulare), one consisting chiefly of non-medullated nerves (neuroma fibrillare amyelinicum), and one consisting chiefly of medullated nerve fibres (neuroma fibrillare myelinicum). He also maintained that many of the recorded cases of neuro-fibromata were in reality true neuromata, composed of non-medullated nerve fibres, on the grounds that the latter, in the absence of special methods of preparation, were very easily mistaken for connective tissue fibres, and also because the disappearance of non-medullated nerve fibres (from pressure) might be the means of a true neuroma being converted into a fibroma, and of its being described and recorded as such. The impression derived from Virchow's teaching is that the frequency of false neuromata has been overstated at the expense of the true neuromata, and that these are of fairly common occurrence. Observations made since 1863, which are the more entitled to our confidence as successive improvements have been made in histological technique, cannot be said to bear out this impression; the neuroma verum is so rare in comparison to the false neuroma, that even its existence has been denied by many, partly on *a priori* grounds, and partly because its occurrence, in their opinion, was imperfectly established. Within comparatively recent years, however, several absolutely authentic cases of true neuroma have been placed on record, so that their occurrence is now accepted

without further question. Since the delivery of Virchow's famous lectures on neuroma, to which reference has been made, the subject has been further complicated and extended by the elaboration of the so-called plexiform neuroma described especially by Verneuil and Bruns, the demonstration of the nerve element in cutaneous fibromata or molluscum fibrosum by v. Recklinghausen, and of the same element in certain forms of elephantiasis and giant growth by Czerny, Hürthle, Nauwerck, Max Jordan, and by Esmarch and Kulenkampf, and also by the accumulating records of cases illustrating all sorts of combinations of nerve tumours with pigmentary and other lesions of the skin. The occurrence also of malignant tumours of nerves, which does not seem to have been properly recognised by R. W. Smith and his predecessors, is not only established in the form of primary solitary independent tumours, but as occurring also in individuals the subject of multiple neuro-fibromata, and described by Garré under the somewhat vague designation of "Secondary Malignant Neuroma." Opinion has also changed with regard to the so-called multiple neuromata, based on the repeated observation that the disease was less of a tumour growth than a widely disseminated fibrosis of the sheaths of the nerves, this change of opinion being illustrated in the adoption of the name "neuro-fibromatosis," in preference to that of multiple neuro-fibromata. The group described by R. W. Smith as "Traumatic Neuromata" has also undergone considerable modifications; originally employed by him to include all forms of tumours or swellings which developed in relation to a nerve after an alleged injury (such as a blow or a squeeze), whether the connection between the injury and the tumour was established or not, the term has come to be restricted to cases in which such a connection is beyond question, viz., in which the nerve is definitely injured, either partially or completely divided, or the seat of a foreign body, or is included in a ligature. In this restricted sense the stump-neuro-

mata are the best known examples of the traumatic neuroma; they have been successively and alternately regarded as true neuromata (and by some authors as the only true neuromata) and as fibro-neuromata, so that even at the present day their exact pathological status has not been defined. Great confusion has resulted from the complication and overlapping of the lesions which fall to be discussed under the general heading of neuroma and the difficulties of classification have been the subject of remark by more than one author. Courvoisier[1] regarded the adoption of an anatomical classification of neuromata as impracticable, and proposed the following mixed classification :—

1. Division neuromata—Amputation and other divisions of nerves.

2. Tubercula dolorosa—Solitary, multiple.

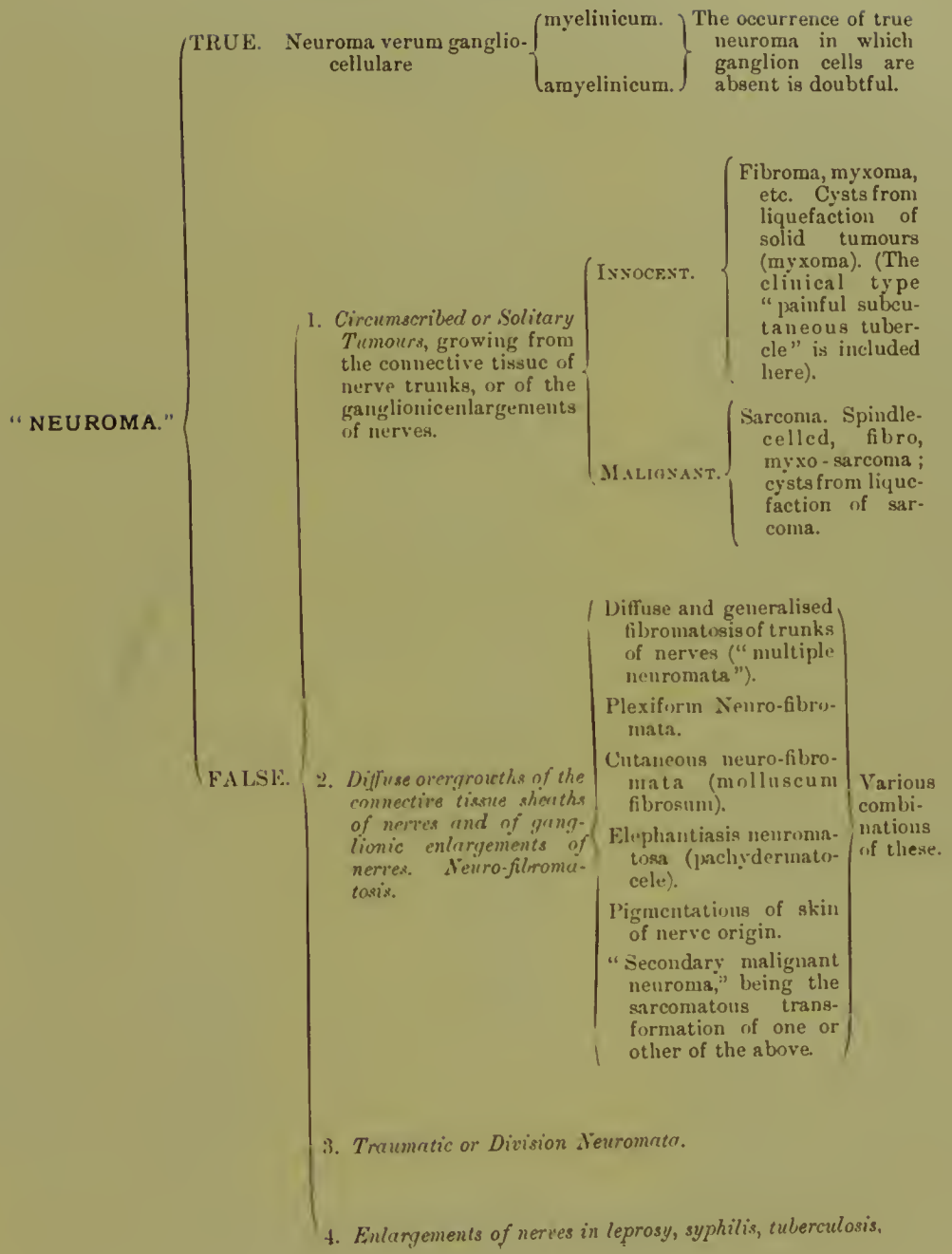
3. Trunk neuromata—Solitary, multiple, local, regional, symmetrical, general.

4. Plexiform neuromata.

The author ventures to propose the following classification, based on the anatomical structure of neuromata :—

[1] L. G. Courvoisier. "Die Neurome." Eine klinische Monographie. Basel, 1886.

Classification of Neuromata



CHAPTER II

THE TRUE NEUROMA

In the sense in which this term was introduced by Virchow, it implies a tumour which is mainly composed of newly-formed nerve tissue, or a tumour, into the composition of which newly-formed nerve tissue enters as an essential constituent. The number of authenticated cases which comply with this definition is indeed very limited. By authenticated, is meant those in which the author's opinion as to the exact structure and nature of the tumour has been universally accepted. They are necessarily those which have been investigated within recent years by reliable histological methods. The author has thought it wiser to exclude from this category the often-quoted cases of Klebs, Czerny, v. Winiwarter, Bruns, Soyka, and Courvoisier, on the grounds above stated, and to exclude also certain other cases in which the presence of nerve cells might not be the result of new formation, because of the tumours in question being situated upon nerves in the vicinity of normally placed ganglia. There are five authenticated cases upon which the following account of the true neuroma is based, in all of which the tumour or tumours were composed of newly-formed ganglion cells, and of nerve fibres both medullated and non-medullated, constituting the neuroma verum gangliosum myelinicum and amyelinicum of Virchow. Inasmuch as it is difficult to conceive of the formation of new nerve fibres in the absence of nerve cells, it would appear to be impossible to admit the occurrence of neuromata exclusively composed of nerve fibres, such as are referred to by Virchow under the name of "neuroma fibrillare" (amyelinicum

and myelinicum). These could only be accepted as possibilities on the assumption that they possessed nerve cells in the first instance, and that the latter disappeared at a later period by some retrograde metamorphosis.

With one doubtful exception all the authenticated cases of true neuroma are connected with the sympathetic nervous system, three of them originating from the main cord or the plexuses within the thorax and abdomen, and the fourth from the minute ganglia on the terminal fibres of the sympathetic nerves accompanying the blood and lymph vessels. As might have been expected in tumours originating from the sympathetic system, there are large unipolar nerve cells in great number, there is a predominance of non-medullated nerve fibres, while the medullated fibres, which are in the minority, are of a more delicate structure than the majority of those met with in the cerebro-spinal nervous system. The medullated fibres may be derived from the non-medullated fibres by the addition of a medullary sheath, as is observed in normal development; others of them merely represent the medullated fibres which normally traverse the main trunk and plexuses of the sympathetic, and are originally derived from the cerebro-spinal nerves. So far as one may venture to make further generalisations from so limited a series of cases, it may be said of the true neuromata that they may present themselves in childhood, or at any subsequent period up to the time (about the age of thirty) when the sympathetic nervous system reaches maturity. The cause of their development is quite unknown. They may be solitary or multiple, circumscribed or diffuse. They vary in size from that of a pea up to that of a child's head. They are unattended by any symptoms which might indicate their nervous origin and structure, being free from pain and quite insensitive. Although they may be diffuse, and to a certain extent infiltrating, and may attain a prodigious size, they are innocent in character.

Their consistence varies from the soft elasticity of a lipoma to the firmer solidity of a uterine myoma. Their situation is more commonly in the main trunk or abdominal plexuses of the sympathetic, less frequently in the subcutaneous cellular tissue. They present difficulties in diagnosis which will rarely be overcome. Their removal by operation can only be advised when they are causing inconvenience, deformity, or damage to adjacent structures in virtue of their bulk or anatomical situation.

They do not appear to be ever associated or combined with any of the forms of the much more numerous and important class of morbid conditions to be described under the head of Neurofibromatosis.

The following is an abstract of the authenticated cases of neuroma verum :—

1. *Multiple ganglionic neuromata in the subcutaneous tissue of the trunk and thighs.*

This remarkable case is recorded by Dr K. Knauss of Stuttgart. The patient, a girl of eight, had developed, in the third year of her life, a number of subcutaneous tumours over the trunk and upper part of the thighs ; they were never painful or sensitive, but appear to have increased in number and in size since they were first noticed. There were sixty-three tumours in all, irregularly distributed as shown in Plate I. They varied in size from a pea to a small orange, and were firm and elastic in consistence. The larger masses were made up of chains or groups of rounded tumours. The provisional diagnosis was multiple lipomata. A number of them were excised, being easily shelled out from a thin capsule. They had no pedicle or any apparent connection with any nerve. Blood-vessels in varying number entered them on all sides. On section they represented a homogeneous, light yellow transparent

PLATE I.



Multiple true neuromata in the subcutaneous tissue of the trunk and thighs.
Dr KNAUSS' case.

appearance, with white fibrous streaks running irregularly through their substance. On microscopic examination, they were found to be composed of large numbers of ganglionic nerve cells and of nerve fibres, both medullated and non-medullated. In one of the smaller, and presumably more recent tumours, the fibres were exclusively of the non-medullated variety. In the remainder, the non-medullated fibres were distinctly more numerous than the medullated. The latter were smaller than the corresponding fibres in the cerebro-spinal nerves. The nerve cells closely resembled those of the sympathetic ganglia; they were rounded or oval, of considerable size, with granular or clear protoplasm and a round nucleus with clear nuclear substance and a distinct nucleolus. Many of them were directly connected with the non-medullated nerve fibres. None of the cells had more than one process, nor were any of them visibly connected with the medullated nerve fibres.[1] As regards the origin of the tumours in this case, Dr Knauss regarded them as being derived from the minute ganglia on the finest terminal fibres of the sympathetic system, which, as trophic fibres, accompany the blood and lymph vessels. His reasons for this conclusion are as follows:—The tumours were not connected with any visible nerve filaments belonging to the cerebro-spinal nerves, the only connections observed were those with blood-vessels; the similarity in structure between the nerve cells of the tumours and those of the sympathetic ganglia; the predominance of non-medullated fibres, and the fine calibre of the medullated fibres characteristic of the sympathetic nervous system.

[1] Knauss recommends investigating tumours suspected to be neuromata by teasing the specimen, in the recent state, in 1·2 per cent. osmic acid solution in glycerine, since the examination of sections of the hardened tumour is very misleading, especially in the differentiation of non-medullated nerve fibres from ordinary connective tissue.

2. *Large diffuse ganglion-celled neuroma of the left dorso-lumbar sympathetic cord.*

This tumour, the largest true neuroma on record, is described by Dr Otto Busse. The patient, a well-developed boy, aged four, had suffered since infancy from partial paralysis of the lower extremities (the right leg being more affected than the left), from dribbling of urine, and want of control over the anus. There was found on examination a large tumour situated on the left side of the vertebral column, extending downwards so as to fill up the greater part of the false pelvis, and upwards, not only beneath the ribs, but also between the ribs and the skin. The tumour was slightly movable, was solid, firm, and of smooth rounded surface. On the left side there was paralysis of the tibialis anticus, and of the extensor communis digitorum; on the right side, of the ilio-psoas, sartorius, quadriceps, adductors, tibialis anticus, and extensor communis digitorum, representing a lesion of the fourth and upper half of the fifth lumbar segments. The tibialis anticus and extensor communis digitorum of both limbs did not react to electricity. There was no alteration in the sensory functions. The tumour was diagnosed as a fibroma or neuroma pressing on the spinal cord. At the father's request, Dr Kredel of Hanover made an attempt to remove it. This was only partially successful; portions were removed in a piece-meal fashion, amounting to 700 grms. in weight. The tumour tissue resembled a fibro-myoma of the uterus. The absence of vascularity was very remarkable. The wound healed rapidly and well. The nerve symptoms were unaltered. Mieroseopic examination of the tumour showed it to consist of nerve fibres, mostly of the non-medullated variety, and of large ganglionic nerve cells. Dr Busse concluded that it originated in the dorso-lumbar sympathetic cord. Although innocent in character, it was imperfectly encapsu-

lated, and might be described as infiltrating the adjacent muscles and fat.

Dr Busse remarks on the difficulty of explaining the paralytic phenomena in this case. The fact of the motor paralysis being more extensive on the side opposite to that occupied by the tumour, and the absence of sensory disturbances, prove that the paralysis was not the result of pressure on the adjacent cords of the lumbo-sacral plexus. He inclines to ascribe the paralysis to an independent partial lesion of the spinal cord (fourth and fifth lumbar segments), the nature of the lesion being undetermined.

Busse regards the tumour here described as allied to the plexiform tumours of the spinal nerves, inasmuch as it was not an isolated tumour, but a diffuse growth, involving the entire abdominal portion of the sympathetic.

3. *Ganglion-celled neuroma of the supra-renal plexus.*

Dr Martin B. Schmidt observed this tumour in making a post-mortem examination on a man aged thirty-seven, who had died of cancer of the stomach. It was situated between the left kidney and supra-renal capsule, and was about the size of a man's fist; it was soft in consistence, and of a greyish-red colour; the supra-renal capsule was fused with the anterior wall or capsule of the tumour. Microscopically it consisted of non-medullated and of a smaller number of medullated nerve fibres, and of ganglion cells. Schmidt regarded the tumour as a true neuroma, originating in the supra-renal plexus of the sympathetic.

4. *Ganglion-celled neuroma of the dorsal sympathetic.*

Loretz records the case of a woman aged thirty-five, who was admitted into hospital in a fit of epilepsy and died. There was a tumour the size of an egg to the left of the second and third dorsal

vertebræ covered by the costal pleura ; it consisted of apolar and unipolar ganglion cells, partly isolated and partly arranged in clusters, and of non-medullated and of a few medullated nerve fibres.

5. *Ganglion-celled neuroma of ala of nose.*

Axel Key records the case of a man aged thirty-one, who developed within a year a tumour the size of a plum on the left ala of the nose. It was encapsulated, greyish-red, soft, like a sarcoma, and was connected with a nerve, probably a branch of the infra-orbital, and contained large apolar nerve cells.

CHAPTER III

OVERGROWTHS OF CONNECTIVE TISSUE ORIGINATING IN THE PERIPHERAL NERVOUS SYSTEM, INCLUDING THE SO-CALLED FALSE NEUROMATA

This heading is, unfortunately, the only one capable of including the important groups of morbid conditions related to nerves which are now to be considered. These have been individually mentioned and grouped in the author's classification given on page 7.

1. *Circumscribed or Solitary Tumours (False Neuromata), growing from the Connective Tissue Framework of Nerves, and of the Ganglionic Enlargements of Nerves.*

The view entertained by the author that these constitute a distinct and separate class of the false neuromata may not meet with general acceptance. On the one hand, the tumours included in this group are not invariably solitary, and on the other, transition forms may yet be discovered between them and the multiple neuromata (neuro-fibromatosis). The latter objection is not an important one, as the occurrence of transition forms between two or more groups of pathological conditions, may not be incompatible with their differentiation into separate classes. The former objection is more apparent than real. The distinctive feature of the members of the group under consideration, does not consist in the tumour being invariably solitary, but in the absence of any general disease, or tendency to disease, in the

peripheral nervous system, such as the neuro-fibromatosis which constitutes the essential lesion in the group which includes the multiple neuromata. In those at present under consideration, the tumour, whatever its nature, involves a nerve which is otherwise healthy.

The tumours belonging to this group are composed of various types or modifications of connective tissue, originating in the elements of the nerve sheaths (endoneurium, perineurium, and epineurium).[1] They resemble similar tumours originating in other tissues and organs. The tissue of which they are composed presents no peculiarity by which the nerve origin of the tumour can be identified. The nerve trunk, which is the seat of the tumour, does not present any pathological changes, other than those referable to the presence of the growth; the nerve fibres remain passive; there is no new formation of nerve fibres; at the most there may be some increase in length where they are bulged or stretched over the tumour. Degeneration and destruction of the nerve fibres, which is very common in the malignant growths, is only met with under very exceptional conditions in relation to the innocent tumours. Nothing is known of their causation, beyond that which applies to tumours in general; at the same time many authors associate the development of these tumours with definite injuries, *e.g.*, bruises, strains, punctured wounds.

The solitary and circumscribed tumours of nerves may be classified according to their anatomical structure, as follows:—

1. *Innocent.*—Fibroma, myxoma, lipoma, angioma, lymphangioma. Cysts from liquefaction or hæmorrhage in relation

[1] As the terms employed to indicate the sheaths of a nerve trunk are employed differently by different writers, it may be as well to state that the term "endoneurium" is used here to indicate the delicate connective tissue between the individual fibres of a nerve bundle; "perineurium" to indicate the laminated fibrous tissue surrounding one or more groups of nerve fibres; while "epineurium" is the general sheath enveloping all the bundles of the nerve.

to these. (The "painful subcutaneous tubercle" is included in this class.)

2. *Malignant.* — Sarcoma. Spindle-celled, fibro, and myxo-sarcoma. Cysts from liquefaction or hæmorrhage in relation to these.

The innocent tumours include all forms of connective tissue tumours capable of originating in the sheath of a nerve trunk. The fibroma and myxoma, or combinations of these, are the only ones commonly met with. The fibroma presents the usual appearances of a definitely circumscribed encapsulated tumour, composed of a firm, glistening, white or pinkish-white tissue; the fibres are arranged in whorls and in interlacing bundles, with spindle-shaped connective tissue corpuscles between them. The proportion of fibres and cells varies in the harder and softer varieties of fibroma. The blood-vessels are well formed. Myxomatous degeneration is met with in scattered areas of the tumour, or the whole tumour may present the soft gelatinous character of a myxoma. The capsule, like that of all tumours originating within a nerve trunk, is derived from, and is continuous with the general sheath of the nerve, and presents a shining appearance externally.

Cysts containing variously coloured gelatinous fluid or semi-fluid material are derived from the solid tumours, and especially the myxoma, by a process of liquefaction, or as the result of hæmorrhage into their interior. The "blood-cyst" of nerves arises in this way. The whole tumour may be converted into a cyst, or several cyst-like cavities may be scattered through its substance. The solid innocent tumours grow very slowly, and seldom attain the size of a hazel-nut; they have been known to remain unchanged for upwards of eighteen years (Wood), and thirty years (Courvoisier). This stationary tendency has earned for them the name of "permanent tumours," employed by Virchow. The cystic varieties may increase in size more rapidly; there are cases recorded of

blood-cysts as large as an orange. The common shape of the solid varieties is that of a flattened ellipse like a lentil or bean, or of an ellipse or sphere, more rarely annulated or lobulated. The relation of the tumour to the bundles of nerve fibres of which the nerve trunk is composed, varies according to whether the growth has originated in the epineurium, perineurium, or endoneurium. The nerve fibres may be spread out more or less equally all round the tumour (central neuroma), or only on one side (eccentric neuroma), or the nerve trunk may run down on one side of the tumour without any dispersion of the nerve bundles (lateral or peripheral neuroma). The tumour may be loosely held within its sheath, so that on splitting the latter it is easily shelled out, or it may be adherent to it, so that the complete removal of the tumour may require time and care.

With the exception of a very limited number of cases, in which the tumour has been regarded as an enlarged Pacinian body, they are met with in the course of nerves, rather than at their peripheral terminations. So far as the author is aware, there is no authentic observation of the occurrence of degeneration in the nerve fibres in any case of innocent solitary neuroma; cases will be referred to, however, in which there was clinical evidence of motor paralysis such as would lead one to suspect the occasional occurrence of such degeneration.

The Anatomical Situation of the Solitary Tumour.

When the tumour is subcutaneous, and is related to a small, unimportant, or unrecognised branch of a sensory nerve, the appropriate name, "painful subcutaneous tubercle," introduced by Wood, is applied to it. On the other hand, when the tumour is related to a larger or more important and definitely named nerve, or one of its branches, it is called a "trunk neuroma." It is obvious

that no hard and fast line can be drawn between these two clinical types of tumour, and that to separate them into distinct classes, as has hitherto been the custom, is not only an arbitrary proceeding, but a method of classification which can only give rise to confusion. A tumour of the internal cutaneous nerve, for example, might be a "trunk neuroma" in the upper arm, and a "painful subcutaneous tubercle" in the forearm, and yet be essentially the same in either situation. Even the exponents of the view that the "subcutaneous tubercle" is a definite entity, have been in the habit of including under the term tumours which are not subcutaneous at all, viz., those on minute and unnamed nerve filaments in the periosteum of bones, and in the capsule of joints.[1]

For facts relating to the topographical distribution of the innocent tumours of nerves, we may quote from Wood, who collected thirty-five cases of subcutaneous tubercle, of which twenty-two were seated in the lower, and eleven in the upper extremities, one in the chest wall, and one in the scrotum. In the larger series of similar cases collected by Courvoisier, the lower extremity was also the commonest situation.

Of the named sensory subcutaneous trunks affected with false neuroma, the author has personally observed cases in the external saphenous above the ankle, the same nerve on the back of the leg, the internal cutaneous in the upper arm and in the forearm, and in the lateral cutaneous branch of the second intercostal nerve (*vide* cases, p. 30). According to Courvoisier, they are met with in the mixed nerves of the limbs in the order of median, ulnar, sciatic, and musculo-spiral.

Solitary innocent tumours, involving the ganglionic enlargements of nerves are so rare, that the author has not been able to collect any reliable information regarding them.

[1] The painful lumps in the breast, included with the neuromata by older writers, are probably the result of chronic interstitial mastitis.

Clinical Features of the Innocent False Neuromata.

These have been so accurately described by the older authors, and especially by William Wood, that at the present day there is but little to be added to the classical description given by him in 1829.

Circumscribed innocent tumours in relation to nerves would appear to affect otherwise healthy adults; in many cases the patient may be described as neurotic, as liable to neuralgic pains, and as bearing pain badly. Although not confined to any particular age, they are more common between twenty and forty. The liability according to sex is, on the whole, fairly equally divided, with a majority, however, in favour of the female. The patient draws attention to a tumour, or to a particular area of the body which is sensitive, and from which pains may radiate to distant parts. If there be a visible or recognisable tumour, the patient may have known of its existence for years before it gave rise to symptoms, or it may only have been noticed when the symptoms directed attention to it. Unless the tumour be very small, and involve a deeply seated nerve (*e.g.* the posterior interosseous nerve in the forearm), it is usually easily identified as the source of the symptoms complained of. Whatever its consistence, size, or anatomical situation may be, the striking features are the sensitiveness of the tumour, and the pains which radiate from it. It may be so sensitive as to interfere with the palpation, which is usually permitted and desired in the clinical examination of tumours. The friction of the clothes or of the stocking may be described as intolerable. The pain excited by manipulating the tumour, generally radiates to the peripheral distribution of the nerve affected, and in this way the latter may be identified; in several cases in which the ulnar nerve was implicated, the pain was distinctly referred to the ring and little fingers. There are certain sources of fallacy here, however, for the pain may not

follow the nerve specially affected, but may be transmitted to other cutaneous filaments with which it communicates; there are cases also in which the pain has been referred to another nerve, because the latter happened to be pressed upon by the tumour. The best example of this is a case recorded by Hume of Newcastle, in which a tumour of the internal popliteal nerve caused pain down the outer side of the leg and ankle, through pressure of the tumour on the external saphenous nerve. There may be also spontaneous pains starting from the tumour, and resembling neuralgia, lasting from a few minutes to an hour or more, or they may be continuous, with exacerbations. They may recur at regular intervals, like malaria. They are influenced or excited by pressure, by movements of the limb (either by the contracting muscles pressing on the tumour, or by the nerve being put upon the stretch), by the advent of changes in the weather, by the recumbent posture or dependent position of the limb, by warmth in bed (interfering with sleep), and by menstruation and pregnancy. The sensitiveness and pain may vary from time to time from unknown causes. According to Wood, some patients "are sensible of an increase in size of the tumour during the attack of pain, and some of them have observed, at the same time, a degree of discoloration of the skin covering the tumour, which became of a purplish or bluish tinge." This would indicate some association between the characteristic symptoms, and alterations in the circulation both in the tumour and in the nerve affected.

The pains have been described as radiating towards the periphery; cases are met with, however, in which the pain shoots towards the trunk (*vide* illustrative cases). Wood also mentions that occasionally "when a smart blow is given to the diseased part, the pain is rapidly extended to different parts of the body, like a shock of electricity."

As illustrating the sudden onset of symptoms in a previously quiescent tumour, the author may refer to one of his cases in

which the patient, a farmer, suddenly felt a stinging pain over his chest, and thought a bee had crept up under his clothes. He discovered the tumour on examining the seat of pain.

Pressure on the nerve trunk above the tumour may arrest the pain, or may excite it; in the latter case, the pain is referred to the tumour.

In tumours involving the larger mixed nerve trunks, there is, on the whole, less liability to pain than when the smaller cutaneous and purely sensory filaments are affected, because the larger nerve trunks are relatively poorer in sensory fibres, they are less exposed to thermal and mechanical influences, and their fibres are more extensible (Virchow). In a nerve trunk, usually described as purely motor in function, there may be, however, the most exquisite sensitiveness in addition to severe pains excited by pressure. In a case observed by the author involving the posterior interosseous nerve in the middle of the forearm, pains were excited even by a dependent position of the limb, and were severe enough to cause a feeling of weakness in the hand, so that the patient, a muscular youth, was unable to grasp anything so long as the pain lasted. The sensory nerve fibres involved in this case, were derived from other tissues than the skin. There is this difference, however, when a purely motor nerve is implicated by a tumour, that the pain is localised to the area of the tumour, and does not shoot down the peripheral distribution, as it does when sensory cutaneous fibres are implicated. In the rare cases in which minute sensitive and painful tumours have been described as occurring in the periosteum and capsule of joints, the pain was also quite localised.

The powers of sensation and of voluntary motion are, in general, very slightly impaired, unless by the severe pain which may result from attempted movements of the limb.

Disordered sensations may, however, be present in the shape

of formication, pins and needles, as if the limb were "sleeping," especially during the attacks of pain. There is never any definite anæsthesia.

Motor disturbances have been occasionally observed in the shape of twitchings, jerkings, or cramps, during the severe attacks of pain, but especially on squeezing or on handling the tumour. The muscles which jerk are not necessarily those supplied by the nerve which is involved in the tumour. For example, the quadriceps extensor may contract when a tumour of the sciatic is compressed. Actual motor paralysis and alterations in the electric reactions are quite exceptional, and probably never result from the pressure of the tumour itself upon the nerve fibres. Injurious pressure on the motor fibres can only occur in certain anatomical situations, *e.g.* where the nerve passes through a bony foramen, or is otherwise exposed to mechanical pressure. Among the illustrative cases there is one recorded by Zum Busch, in which a tumour the size of a walnut, situated about three fingers' breadth above the internal condyle, and in the vicinity of an old fracture of the humerus, caused paralysis of the ulnar nerve, and atrophy in the hand muscles supplied by that nerve, which disappeared four weeks after removal of the tumour in question. Various trophic and vaso-motor disturbances have been incidentally mentioned by different observers, *e.g.* œdema, sweating, changes in the temperature of the limb. Wood and others mention also the very occasional occurrence of epileptiform convulsions, which have disappeared after the removal of the tumour.

Diagnosis of Innocent Solitary Tumours.

It is usually easy to recognise the nerve origin of any tumour by the characteristic clinical features. In the trunk-neuromata, further assistance is obtained from the tumour being situated in

the course of a nerve, and by its admitting of no motion in a longitudinal direction. A difficulty sometimes occurs in distinguishing tumours originating in structures in the vicinity of a nerve from those arising in the nerve itself, as, from the proximity of situation, the symptoms may be very much alike. The diagnosis may sometimes be made by careful criticism of the symptoms, and more particularly, by observing the effects of pressure on the tumour in different positions of the limb. Pring records a case of suspected tumour of the ulnar nerve at the elbow, in which the tumour could be displaced over the epicondyle, in which position it could be freely handled without causing pain.

Treatment.—If the tumour be the source of suffering, it should be removed. If it be in the subcutaneous tissue, or in a purely sensory nerve, the operation may be undertaken without having any regard to the nerve from which it is growing. In the mixed or purely motor nerves, every respect must be shown to the nerve fibres. When the tumour is exposed, the capsule is to be divided longitudinally, and the tumour shelled out therefrom. With one or two exceptions, in which the pain has been temporarily aggravated by the operation, the pains and other symptoms disappear at once. Anæsthesia in the area of distribution of the nerve which has been interfered with, and in the case of mixed or motor nerves, a minor degree of paresis or paralysis, is occasionally observed, but it is usually temporary and soon disappears. If the tumour is really innocent, there should be no question of recurrence. Courvoisier has collected one hundred and twenty-four cases in which a tumour was removed, with six recurrences; these were probably instances of incomplete removal, since a second operation was successful in bringing about a cure. There may be exceptional cases in which, in order to remove the tumour completely, it may be necessary or desirable to resect a portion of the affected nerve along with it. The continuity of the divided nerve trunk

must then be restored by one or other of the recognised methods of procedure; if the wound be aseptic, complete recovery of function may be confidently anticipated. This subject will be further referred to in considering sarcoma of nerves.

2. *Primary Malignant Tumours, growing from the Connective Tissue Framework of Nerves, and of the Ganglionic Enlargements of Nerves. Malignant Neuromata.*

The primary sarcomata of nerves originate as such, or they may result from the malignant transformation of a tumour which was previously innocent. They nearly always partake of the fibro, myxo, or spindle-celled type. They frequently contain cysts, of variable number, size, and contents. They grow with varying rapidity, and may attain a considerable size, from that of a walnut to that of a child's head. Like the corresponding innocent tumours, they may originate in the epineurium, perineurium or endoneurium, and occupy a variable position in relation to the bundles of nerve fibres. They may appear to be encapsulated. Unlike the innocent tumours, however, they exert injurious pressure upon the nerve fibres, and lead to their actual destruction and replacement by the cells of the tumour. When the latter gain access to the interior of one or more groups of nerve fibres, enclosed in the special perineurium, they propagate themselves continuously in the long axis of the nerve, presumably in the lymphatic spaces surrounding the nerve fibres, for a varying distance, in a manner which is quite characteristic. As a result of this, the tumour is irregularly lemon-shaped, its poles tailing off gradually above and below into the nerve trunk to which it belongs; between the two poles the nerve may, or may not be recognisable on the free surface. The nerve is obviously thickened as it enters and as it leaves the tumour, and is really infected

beyond the visible limits of the tumour. In transverse sections of the thickened nerve (whether entering or leaving the tumour), the perineurium which originally enclosed bundles of nerve fibres may be found entirely occupied or filled with sarcomatous cells. In transverse sections through the tumour itself, certain nerve bundles may be seen, displaced and scattered, for the most part towards the periphery or surface of the tumour, others are entirely surrounded by tumour tissue, while others again show the remains of the perineurium enclosing sarcoma cells, which are crowding the nerve fibres to one side, or causing their actual disappearance. In addition to these features, which are peculiar to sarcomata originating within the trunks of nerves, there are others resembling those of sarcomata in other organs and tissues, viz., the tendency to infiltrate and invade the surrounding tissues. Originally invested, like the innocent tumours, by the external sheath of the nerve, they excite what may be regarded as reparative changes in the adjacent structures, whereby these become adherent to the tumour. This specially affects the muscles and the sheaths of the blood-vessels which may accompany the affected nerve trunk. Following insensibly on this adhesion of the tumour with the adjacent structures, the cells of the tumour erupt through its capsule, invade the surrounding tissues, and may ultimately reach the skin and fungate externally. In a limited number of cases, they infect the lymphatic channels, and give rise to secondary growths in the lymphatic glands. More commonly, the tumour cells erupt into the lumen of blood-vessels, and give rise to metastases in distant organs, *e.g.* lung, pleura, heart wall, liver, retroperitoneal glands, etc. In their general malignancy, they approach very nearly to sarcomata originating in the periosteum of the long bones of the limbs.

Clinical Features.—Certain of these are identical with those of the corresponding innocent tumours (q.v.), and need not be further mentioned ; other features are peculiar to the sarcomata.

The majority of the patients are in the prime of life (twenty to forty), and are in perfect health. They tell of the recent appearance of a tumour which is very sensitive, and which is the seat of pains which seriously interfere with their avocation and with sleep. Their sufferings are all of recent date, and are progressive, and their thoughts are concentrated on the tumour. The latter is in the position of one or other of the well-known sensori-motor nerve trunks. In addition to the sensitiveness of the tumour, and the pains associated with it, they may complain of a feeling of numbness, and of loss of power in the extremity affected. On examination, the tumour is readily recognised; its connection with a nerve is usually evident from the symptoms; its malignant characters may or may not suggest themselves at the outset, but will inevitably do so, if the case be kept under observation, either by the exhibition of clinical features common to all malignant tumours, or by the development of symptoms indicative of implication and destruction of the fibres of the nerve involved, sufficient to differentiate it from the innocent neuroma. The onset of jerkings and cramps, the development of motor paresis or paralysis, of wasting of muscles, and of the reaction of degeneration, or other trophic changes, afford strong evidence in favour of the malignant nature of any tumour involving a nerve. Primary sarcomata of nerve trunks (*i.e.* in the absence of already existing neuro-fibromatosis) are decidedly rare. Courvoisier collected fifty-three out of a total of six hundred cases of nerve tumour; but as he apparently included sarcoma developing in cases of multiple neuromata, his figures are not so valuable. The author has collected, in tabular form, the main facts regarding twelve authenticated cases of primary sarcomata of nerves, as follows:—

Primary Sarcomata of Nerve Trunks of the Limbs.

Author.	Age of Patient	Sex.	Nature of Tumour.	Nerve affected.	Operation.	Result.
Berry	19	f.	fibro-sarcoma	left sciatic	tumour removed + 4 in. of nerve	Recovered so as to be able to walk, and then lost sight of.
Bobroff	55	m.	fibro-sarcoma	sciatic	tumour removed + 4½ in. of nerve	Recovered so as to be able to walk ; alive and well 2 years later.
Goldmann	28	f.	spindle-celled sarcoma	left sciatic	tumour removed + portion of nerve	Recurrence; metastases; death.
Hume	40	m.	small round-celled	rt. int. popliteal	tumour removed + 3½ in. of nerve	Recovered and able to walk ; alive and well 5 years later.
Herczel	28	f.	fibro-sarcoma	1st digital brauch of iut. plantar	Chopart's amputation	Recurrence; amputation of leg; died of metastases within a year.
Coupland	34	m.	spindle-celled	left sciatic	tumour removed + 5 in. of nerve	Recurrence ; metastases ; death within 2 years.
Kriege	19	f.	fibro-sarcoma	right median upper arm	removed + portion of nerve and vessels	Gangreue of arm ; amputation at shoulder.
Finotti	26	m.	spindle-celled	right sciatic	tumour shelled out	Recurrence ; removed + 6 in. of nerve, 9 operations in all ; died within 3 years.
Gerster	50	m.		right external popliteal	removed with portion of nerve	Still under observation.
Hume	24	m.	fibro-sarcoma	left sciatic	removed + 6 in. of nerve	Recovered and able to walk ; lost sight of.
Alexis Thomson	29	m.	large spindle-celled	left posterior tibial	removed + 5 in. of nerve and vessels	Recurreuce ; amputation ; death from metastases within 6½ months of first operation.
Alexis Thomson	66	m.	myxo-sarcoma	left musculo-cutaneous in leg	removed + portion of nerve	Recurrence ; amputation ; alive and well 2 years later.

It will be observed from the above facts, that the great sciatic nerve is that most frequently involved; that removal of the tumour along with a portion of the nerve has been the treatment most commonly practised; that while recovery of the nerve functions after this procedure has been remarkably good, recurrence has been the rule (in cases which have been kept long enough under observation), and that death from internal metastases has occurred in the majority of these, in spite of secondary amputation. There are only two cases in which the removal of the tumour, along with a portion of the nerve affected, has resulted in a cure of two or more years' duration. We may therefore conclude that while conservative operations have been successful in a very small proportion of the recorded cases of malignant neuroma (analogous to the results obtained in sarcomata of the long bones of the limbs), that the best, and in the majority of cases, the only chance, lies in early and high amputation; the rationale of this treatment being that we have not only to deal with a sarcoma of pronounced malignant tendencies, but with one which spreads upwards along the interior of the affected nerve trunk. There will remain a certain number of cases which are unsuitable for amputation or any other major operation, and in which it may be desired to mitigate the sufferings of the patient. This may be effected by division or resection of the nerve affected. When it is impossible to do this above the tumour, it would appear to be equally satisfactory when performed below the tumour, the explanation being that the chief source of pain concerns those fibres which are derived from the peripheral distribution of the nerve, and which are injuriously pressed upon as they pass through the tumour.

The occurrence of sarcomata in the ganglionic enlargements of nerves is so very rare, that there are no reliable facts concerning them. There is recorded, among the illustrative cases at the end of this chapter, a remarkable case of what appears to have been a sarcoma of the Gasserian ganglion, quoted from Smith's great work on Neuroma.

INNOCENT TUMOURS

Abstract of Cases which have come under the Author's Personal Observation

1. *Myxoma of right posterior interosseous nerve with excessive pain and tenderness over tumour: excision of tumour: temporary paresis of muscles supplied by the posterior interosseous: recovery.*

T. S., 17, apprentice joiner, Dumfries. Recommended to Professor Annandale by Dr Thomson of Dumfries, and admitted to the Royal Infirmary, 30th November 1896.

Of healthy antecedents, he began to suffer two years ago, without any apparent cause, from pain and tenderness on the dorsal aspect of the right forearm. The pain comes on of itself, or on hanging the arm, but is especially excited by touching the sensitive area. He has been obliged to have the forearm supported in a sling, because when it is allowed to hang the pain begins, and the hand becomes paralysed so that he is unable to grasp anything for some little time (half an hour) afterwards. Liniments and blisters have been applied without benefit, and he has had to give up his work.

On admission he was found to be a very healthy young man, and although of nervous disposition, there was no suggestion of any hysterical or malingering element in his case. On the dorsal aspect of the right forearm, about the centre of its middle third, there was an area which, when touched however gently, caused him intense pain. There was no visible swelling or other alteration of the tissues. On account of the sensitiveness on handling, nothing could be learned from palpation. The diagnosis was that of a small tumour involving the posterior interosseous nerve.

Professor Annandale, on the 3rd December 1896, made a longitudinal incision over the sensitive area, and having displaced the superficial muscles, exposed the posterior interosseous nerve a little

below the point where it emerges from the lower border of the supinator brevis; the nerve was the more easily found because it was partly surrounded by a soft, fusiform, greyish-red tumour, about the size of an almond. The tumour was shelled out, without apparently injuring the nerve. The following day the hand tended to droop, and he was unable to extend the fingers; the pain had entirely disappeared. There was retention for three days, necessitating the use of the catheter. Three weeks after the operation he was still unable to extend the ring and little fingers completely. Thereafter his recovery was quite satisfactory, and he was able to return to work. Two and a half years later, Dr Thomson of Dumfries kindly reported that he was in good health, but that he still complained now and then of a tired numb feeling in the arm after a hard day's work, relieved by holding it under a tap of cold water.

2. *Fibroma of left external saphenous nerve at ankle, very sensitive, and the cause of pains radiating up the leg and down to the little toe: excision of tumour: recovery.*

Miss B., 34, housekeeper, Edinburgh, seen with Dr Murdoch Brown, 20th November 1897. She had always enjoyed fair health. The present trouble began a little over three years ago with severe pains on the outer side of the left tendo-Achillis. About six months later, a tumour was discovered in this situation; it was then the size of a small pea. It pained her at intervals, and especially at the menstrual periods. During the last two years, the tumour has grown larger and has become more sensitive; when handled, the pains shoot upwards along the outer side and back of the leg, as high as the knee, and downwards towards the little toe. While constitutionally healthy, she might be fairly described as neurotic; the tumour was the size of an almond, was subcutaneous, in the groove between the

external malleolus and the tendo-Achillis, but was so sensitive to touch that she would scarcely allow one to handle it. The tumour was shelled out under chloroform on the 21st November 1897; it was found to be composed of a solid, firm, glistening tissue, made up of fibres arranged in whorls with spindle-shaped connective tissue corpuscles between them. The operation was followed by complete disappearance of the symptoms.

The above is a typical example of what was formerly called the "painful subcutaneous tubercle."

3. *Myxoma of posterior branch of internal cutaneous nerve in the middle of the left forearm, giving rise on manipulation of the tumour to pains shooting up and down the arm: excision: recovery.*

S. H., 32, Hebrew teacher, Edinburgh. Sent to me by Dr Norman Walker, 15th May 1896. He had noticed a small swelling on the left forearm about two months ago. Three weeks ago it became very sensitive, so that when anything came against it, it hurt him, and the pain shot up and down the arm. His general health is good, but he is inclined to magnify slight ailments. On the left forearm, about the centre of the posterior ridge of the ulna, and half an inch to the radial side of the ridge, there is a soft movable subcutaneous tumour, about the size of half a cherry. It is very sensitive to pressure, and the pain shoots up and down the forearm. I excised the tumour under cocaine anæsthesia on the 15th May 1896; it was bluish-grey, soft, translucent, and was prolonged at either end into the nerve in which it had originated; the latter was cut across above and below the tumour. The result of the operation was unusual in so far as he suffered from intense pain in the region of the wound for a period of forty-eight hours, during which time he was unable to sleep. He then recovered completely.

4. *Myxo-fibroma of lateral cutaneous branch of second right intercostal nerve, the seat of stinging pains in the tumour itself, and shooting down the inner side of the arm to the elbow: excision: recovery.*

Mr B., 42, farmer, Millerhill. Seen with Dr Belasco, 1st December 1897. About two years ago he felt a stinging pain a little below and to the outer side of the right nipple; he thought a bee had stung him under his clothes. On examination, he found a small lump like a swan-shot, and on handling it the pain recurred. It was always very sore when anything came against it, and if he rolled over on to it in bed the pain wakened him. He is a robust, healthy man. The tumour is situated below, and a little to the outer side of the right nipple; it is subcutaneous, movable, and about the size of a hazel-nut. He literally jumps when it is compressed, and says that the pain shoots down the inner side of the arm as far as the elbow. I excised the tumour under cocaine anæsthesia. The pains disappeared completely. The tumour on section was found to belong to the less cellular type of fibroma; the fibres are arranged in whorls and in interlacing bundles; there are scattered areas of myxomatous degeneration.

5. *Fibroma of lesser internal cutaneous in left upper arm, sensitive, causing pains which shoot down the arm, and upwards on to the chest, and interfering with the use of the arm and fingers: excision: recovery.*

Mrs L., housewife, Edinburgh. Admitted 9th February 1893 to the University Clinical Wards, under the care of Professor Annandale. She has always been healthy; she is the mother of five children. After the birth of her last baby, five years ago, she had eczema of the left forearm, which lasted nine months. About four years ago her attention was drawn to a small lump in the left upper arm by acute pain set up when anything came against

it. The pain radiated down the limb. The lump has not increased in size since it was first observed, but the pains have become aggravated so as to interfere with the use of the arm, and especially of the fingers.

On admission she is found to be a healthy woman. The lump complained of is about the size of a small walnut, situated on the inner aspect of the left upper arm, over the brachial artery, and receiving its pulsation. It is elliptical, with its long axis in the line of the artery. It is soft, freely movable from side to side, and extremely sensitive. The pain shoots down the arm and along the radial side of the forearm towards the thumb; it also shoots upwards on to the wall of the chest, terminating on the outer side of the right nipple. Professor Annandale excised the tumour under chloroform on the 15th February 1893; it shelled out easily from its capsule, the latter was recognised to be continuous above and below, with a small nerve trunk. Recovery was complete and permanent.

The tumour removed was a flattened ellipse, moderately firm, greyish in colour, and gelatinous on section. Microscopically, it was a cellular fibroma, with well-formed blood-vessels, and with patches of myxomatous degeneration. It resembled similar tumours from other situations, *i.e.* there was nothing to indicate its origin from the sheath of a nerve, unless perhaps a want of uniformity in the arrangement of its tissue elements.

Illustrative Cases obtained from other Sources

Circumscribed fibroma of ulnar nerve: excision along with a portion of nerve.

H. Braun of Leipzig reports a case of fibroma of the ulnar nerve, in which 4 cm. of the latter were removed along with the tumour. After stitching the divided ends of the nerve there remained a gap

of 1·5 cm., which was bridged over with several strands of catgut. The wound healed by first intention. At first there was complete paralysis in the area of the divided nerve; later, its functions were completely restored.

Circumscribed fibroma of ulnar nerve: excision: recovery.

Finotti records the case of a railway guard aged thirty-three, who noticed one year before, after a trifling injury, the appearance of a pea-like tumour immediately above the internal condyle of the humerus, which caused him pain, especially at night. The tumour was easily shelled out after splitting the sheath of the ulnar nerve.

Circumscribed fibroma of sciatic nerve: excision: recovery.

Finotti also records the case of a woman, aged twenty-six, who began to suffer two and a half years before from pains on the outer side of the left leg, radiating down to the foot. She then noticed formication and pains down the back of the thigh after sitting on a hard chair. A tumour the size of an egg was discovered at the upper part of the thigh, and found to be very sensitive. The tumour was shelled out and found to be a hard fibroma growing from the outer sheath of the sciatic nerve at the point where the latter emerges from the lower border of the gluteus-maximus. The patient was seen a year later, and was found to be quite well.

Blood cyst of sciatic nerve: excision: recovery.

This case is recorded by Surgeon Lieut-Col. Hatch. A healthy-looking man, aged about forty, complained of a tumour at the back of the left thigh, of ten years' duration. At first it gave him no inconvenience. About a month before admission to hospital it became slightly painful. A tumour the size of an orange was found at the back of the thigh at the junction of the middle and lower third. The skin over it was tense and shining. The swelling was globular,

firm, smooth, and slightly elastic, very movable from side to side but not up and down. If the leg was flexed, the tumour could be moved more readily. The limb was not wasted. Pain was felt in the tumour and down the leg while walking, which made the patient limp a little. There was no tingling sensation. The femoral glands were not enlarged. The flexor muscles were evidently superficial to the tumour, and were spread over it in a thin layer. All the organs were healthy. A longitudinal incision five inches long was made over the tumour; the flexor muscles were dissected off the surface. The tumour was slightly lobulated and had a bluish appearance; towards the lower end a yellow spot was seen, and here there was slight bulging. Continuing the dissection up and down, the swelling was found to be connected with the sciatic nerve; a few veins and nerve fibrils ramified over the surface. A small puncture accidentally made on the surface allowed pure blood to escape with considerable force; the opening was closed with forceps, and the nerve fibrils which were in contact with the surface were very carefully separated on both sides. The sac was then completely evacuated, and the trunk of the nerve, which was spread out on its deep and anterior surface, was defined and the sac removed; a skein of fibres, having been cut near the upper end of the cyst, was sutured. The sac had a thin wall, apparently continuous with the sheath, and contained pure blood, a little fibrin, and hæmatoidin crystals. Recovery was quite satisfactory.

Cyst of ulnar nerve: partial ulnar paralysis: evacuation of cyst: recovery of the paralysis.

Zum Busch records the case of a man aged thirty, who had a movable fluctuating tumour, the size of a walnut, situated about three fingers' breadth above the internal condyle of the right arm, and feeling somewhat like an enlarged and softened lymph gland. It seemed to be close under the skin, which, however, was not adherent over it. There was evidence that the patient had had

in early childhood some fracture about the elbow, possibly a T-shaped fracture of the lower end of the humerus; there was likewise a history of some injury to the elbow five weeks before. The ulnar nerve could be felt below the tumour, and seemed to pass into it. The patient complained of pain in the neighbourhood of the tumour, and there were signs of paralysis of the ulnar nerve and atrophy in the hand muscles supplied by it. An operation was performed, and the tumour was found to be a smooth-walled cyst containing a yellowish, jelly-like material resembling synovial fluid; the ulnar nerve formed an expansion around the cyst wall. The cyst wall was sponged with a solution of corrosive sublimate, and the wound healed by first intention. The patient was treated for four weeks with electricity and massage; the atrophy disappeared, and the function of the ulnar nerve was restored, so that two months after the operation, the man could resume his work as a furniture polisher.

MALIGNANT TUMOURS

Abstract of Cases which have come under the Author's Personal Observation

1. *Large spindle-celled sarcoma of left posterior tibial nerve, very sensitive on handling, attended with severe pains shooting down to the toes: excision of tumour along with the nerve and vessels: recurrence locally and in the femoral glands: amputation of leg and removal of glands: recurrence in groin: extensive operation for its removal: general dissemination of sarcoma: death.*

J. F., 29, miner, Bo'ness. Admitted to the Deaconess Hospital, 20th June 1895, having been sent to me by Dr Roderick Marshall.

The patient has enjoyed the best of health until two years ago, when he began to suffer from occasional pains in the region of the left tendo-Achillis. Six months later he noticed a swelling on the inner side of the tendon, which has grown slowly but steadily ever since. The pains have also become more frequent, and more severe, and latterly have interfered with sleep.

He is a spare muscular man, of a nervous and excitable disposition, complaining very much of neuralgic pains in the left leg and foot which prevent him sleeping at night. There is an evident swelling in the lower half of the leg between the edge of the tibia and the tendo-Achillis; it is divided into an upper and a lower half by a horizontal depression; it extends backwards beneath the tendo-Achillis; it cannot be freely handled on account of its sensitiveness, but it appears to be semi-solid, and it can only be moved from side to side within very narrow limits; the surface tissues are stretched over it. It makes him limp in walking, especially if the feet are bare. The local appearances were quite in harmony with the diagnosis of tubercular tenosynovitis, but the sensitiveness and pains which had been specially observed by Dr Cattanach, then resident physician to the hospital, enabled him to make the diagnosis of tumour involving the posterior tibial nerve.

On the 28th June 1895 I explored the tumour by a free incision, and finding it sarcomatous, removed it, along with the posterior tibial nerve and vessels; the nerve was thickened on entering the tumour above and on leaving it below; it was divided well beyond the limits of the growth. The wound healed rapidly, and he went home freed from his pains and much improved in health. The disability from the extensive removal of the nerve was less than was anticipated. He was able to walk quite well with the aid of a stick. About two months later he came back with recurrence in the scar, and enlargement of the femoral glands. Dr Logan Turner, who was taking charge of the wards in my absence, amputated the

leg, and excised the mass of sarcomatous glands in Scarpa's triangle. After an interval of less than two months, during which time he had gained in weight, there was again a mass of glands in the groin. I performed a very extensive operation for their removal, dividing Poupart's ligament, and resecting the femoral and external iliac veins. He then went down the hill very rapidly with symptoms of secondary growths in the pleura and in the subcutaneous tissue of the scalp and trunk, and died six and a half months after the first operation, and two years and seven months after the original symptoms of the disease. Post-mortem examination revealed disseminated nodules of sarcoma in the pleura, lungs, heart wall, liver, kidneys, retroperitoneal glands, and in the subcutaneous tissue.

The primary tumour was an irregularly lobulated, spindle-shaped mass, tapering off above and below into the nerve with which it was connected. The nerve is markedly thickened where it joins and where it leaves the tumour, but above and below these points it rapidly regains its normal dimensions. Between the two poles of the tumour the nerve is not recognisable on the surface. The tumour has an apparent capsule, with a smooth, shining exterior. The surface is nodular and uneven. On section, the tumour is solid, and is made up of a granular friable tissue of a greyish-white colour. On microscopic examination it is found to be a vascular and very cellular sarcoma; the prevailing type is the large spindle cell. There are areas of hæmorrhage and of degeneration. In transverse sections the displaced and partly scattered bundles of the posterior tibial nerve are seen; they are mostly at the periphery or surface of the tumour, but some of them are entirely surrounded by the growth, so that their perineural sheath is in immediate contact with the cells composing it. In a limited number of bundles the perineurium has disappeared, while in others the spindle cells of the tumour are seen replacing the nerve fibres, and either crowding them to one side, or causing their actual disappearance. The tendency

would appear to be for the tumour tissue, after it has made its way into the interior of a primitive bundle, to extend itself along the bundle and within its perineurium for a considerable distance, for there may be the appearance of an intact perineurium entirely occupied or filled with sarcomatous cells, side by side with others entirely occupied by nerve fibres. It is obvious, therefore, that the enlargement of the nerve immediately above and below the tumour, is due to the prolongation of the sarcoma tissue within the general sheath of the nerve, and not only between the primary bundles of nerve fibres, but in the interior of the bundles themselves, and in contact with and replacing the nerve fibres. Sections of the trunk of the nerve above the tumour show that while the nerve as a whole presents a normal appearance, there is at least one large primitive bundle which may be regarded as the seat of degeneration, inasmuch as the endoneurium, especially around the periphery of the bundle, is considerably increased in amount, and a proportion of the nerve fibres have disappeared.

2. *Myxo-sarcoma of musculo-cutaneous nerve on anterior aspect of left leg: removal of tumour: local recurrence: amputation of leg: recovery.*

J. H., 66, widower, colliery overseer, Dunfermline, was admitted 1st December 1896 into the University Clinical Wards, Royal Edinburgh Infirmary, under the care of Professor Annandale. He had always enjoyed good health until eight months ago, when he felt a sharp pain in the lower part of the left leg. Some days later he noticed a lump on the front of the leg. In the course of six months it had grown to the size of a man's fist. The pains originally complained of became very much worse, especially during the night; he sometimes had to get out of bed and sit on a chair for the greater part of the night. The pain used to shoot down the front

of the leg as far as the toes, especially the great toe and the one next to it. Dr Bell of Dunfermline removed the tumour eight weeks ago, but after a period of relief from pain, during which the leg felt numb, the tumour grew again.

On admission he was found to be a robust, well-preserved man. There is a linear scar six inches long on the anterior aspect of the left leg, adherent to, and bulged by a swelling beneath ; the swelling is elliptical, soft or semi-fluid, fixed to its surroundings, as well as to the overlying skin. It is only slightly tender on pressure. There is none of the old pain shooting down to the toes. There is no definite anæsthesia such as would correspond with the removal of the musculo-cutaneous nerve at the first operation. The diagnosis was made of recurrent sarcoma, which had apparently originated in the musculo-cutaneous nerve.

Professor Annandale amputated the leg by a posterior transfixion flap at the level of the tubercle of the tibia. On dissecting the limb after its removal, the tumour was found to be very soft and gelatinous, with scattered areas of hæmorrhage and yellow degeneration. It was adherent to the overlying skin, and it infiltrated the adjacent extensor communis digitorum and extensor hallucis muscles. The internal trunk of the musculo-cutaneous nerve was traced into the tumour which it entered obliquely about one inch below its upper rounded pole. No nerve was found at the lower pole ; it had evidently been removed at the first operation. The absence of any motor paralysis is accounted for by the branches to the peroneus longus and brevis being given off above the level of operation. The other nerves of the limb were normal. The microscopic examination of the tumour showed it to be, for the most part, a typical myxoma ; large branching, and some multinucleated cells, in a jelly-like matrix, with fairly well-formed blood-vessels ; here and there, however, the cells were more numerous and more closely packed, and were evidently in a stage of transition to sarcoma.

A fortnight after the patient went home, he was admitted to the Cottage Hospital at Dunfermline under the care of Drs Drysdale and Tuke, and on their advice, underwent amputation through the middle of the thigh. Two years later, he was known to be alive and well.

Fibro-sarcoma of the right brachial plexus above and below the clavicle: exploratory operation: gradual increase in size.

I. M., girl, aged seventeen, Edinburgh, seen at her own home with Dr Graham, 16th October 1898. Apart from bilious attacks, she had always enjoyed good health. About two years ago, she began to complain of pains shooting down the right arm, and of pain in the shoulder on fitting on a new bodice. Two months later she accidentally noticed a lump in the neck just above the right collar-bone. It was not sensitive at this time. She attended as an out-patient at a hospital, and complained of the pains in her arm. On inquiry as to the existence of any lump, she showed the one above the clavicle. A series of blisters were applied without benefit. She was then admitted to the hospital, and the lump in the posterior triangle which was supposed to be a tubercular gland, was explored on 17th June 1897. A tumour was found involving the cords of the brachial plexus; the wound was closed. She was relieved from pains for over two months; they then returned and have become more severe, being always worse at night, so that she has to get up from her bed and walk about the room. Although the tumour has increased in size, her general health remains excellent. When I saw her on 16th October 1898, sixteen months after the exploring operation, and two years from the first onset of symptoms, she presented a tumour which projected above and below the right clavicle; the upper and more prominent portion was about the size and shape of a lemon, and there was a wide irregular scar in the overlying adherent skin; the portion of the tumour below the clavicle was more recent and less prominent. She objects to any handling of the tumours. When gently pressed, the pains shoot down to the

elbow, when pressed firmly they shoot down to the fingers, and especially to the thumb. These pains differ from those which come on of themselves; the latter are less severe, they only extend to the middle of the forearm, and very occasionally to the thumb, and are relieved by inclining the head to the affected side, and raising the elbow with the other hand. Movements of the arm above the level of the shoulder, such as dressing her hair, excite the pains, so that she may have to stop in the middle of it.

Palpation of the tumours is unsatisfactory, as even light touching of the skin over them causes pain. The upper tumour occupies the entire supra-clavicular space from the sterno-mastoid to the trapezius; it dips in deeply behind the former to the transverse processes of the sixth and seventh cervical vertebræ. It is quite fixed and matted to the surrounding tissues. It appears to be elastic or semi-fluid in consistence. The tumour below the clavicle is quite as large as the upper one; being beneath the pectoral muscles it is best felt from the axilla, as a fixed, solid tumour; it is distinctly less sensitive and can be handled more freely.

The superficial veins are dilated all over the region of the shoulder. There is no apparent atrophy of the muscles of the shoulder or arm. Her usual attitude is one of left dorsal scoliosis, with the right shoulder considerably higher than the left; it is evidently assumed to relax the parts in the posterior triangle, especially the trapezius and levator anguli scapulæ. The other nerve trunks of the body are healthy. There are no skin lesions.

She was seen again on 25th August 1899. Her general health is almost the same; she thinks she is more easily tired; the pains trouble her as before; she cannot raise the elbow to the level of the shoulder. The tumour above the clavicle has not changed; that below the clavicle is much larger, more hemispherical, and the subcutaneous veins over it are more prominent. Both tumours are quite as sensitive as before.

Cases Abstracted from other Sources

Large fibro-sarcoma of the sciatic nerve: removal: recovery.

Mr James Berry, of the Royal Free Hospital, London, reports the case of a woman aged nineteen, who had noticed, eighteen months before, a tumour the size of an egg on the posterior aspect of the left thigh; eleven months later she experienced slight pain and numbness on sitting. The patient began to lose flesh as the tumour increased in size. The tumour extended from the level of the trochanter to just above the knee joint. Its upper part was covered with the hamstring muscles; it was tender on pressure. The motor functions were normal. The tumour was freely exposed by division of the overlying tissues; the great sciatic nerve was entirely surrounded by it; the hamstrings were infiltrated at the upper part, and were extensively removed. Four inches of the nerve were removed along with the tumour, and as it was impossible to bring the divided ends together, they were cut short above and below. The growth with the muscles attached, weighed 6½ lbs. Microscopic examination showed it to be a fibro-sarcoma. The wound healed well. The limb was at first quite powerless below the hip joint, but she recovered the power of flexing the knee by the sartorius; sensation was intact along the inner aspect of the leg and heel; the rest of the foot and the outer part of the leg were insensitive. A fortnight later, sensation had returned except on the outer aspect of the leg. A gutta-percha splint was applied to prevent foot-drop. She was able to walk with crutches, and later with the aid of a stick, and finally without any assistance. The patient was afterwards lost sight of. Mr Berry remarks on the slight amount of pain caused by the tumour, and on the comparatively slight degree of malignancy which it presented.

Fibro-sarcoma myxomatodes of the sciatic nerve: removal: recovery.

Bobroff removed this tumour along with 12 cm. of the nerve from a man aged fifty-five. The initial disability of the limb recovered to such an extent that two years later he was able to use the limb very satisfactorily.

Spindle-celled sarcoma of left sciatic nerve: excised with a portion of the nerve: recurrence of the growth and internal metastases.

Edwin Goldmann of Freiburg, reports the case of a woman aged twenty-eight, who had noticed a tumour in the left thigh six months before, and who also complained of severe pains shooting down to the foot. The tumour was as large as an orange, and was painful on pressure. When the hip was flexed while the knee was extended, she suffered severe shooting pain. The tumour was removed by Kraske, along with a portion of the sciatic nerve, the fibres of which were spread out over its surface. After the operation the patient could still flex the knee; the leg and foot were completely paralysed. There was anæsthesia on the outer aspect of the leg, the inner and under surface of the foot, and over the greater part of the dorsum of the foot. Rapid and painless recurrence took place, which was removed by operation. The tumour again recurred, and the general health failed in a way suggestive of metastases in the internal organs.

The tumour was found to be a spindle-celled sarcoma, originating in the endoneurium of two of the nerve bundles, the fibres of which were almost completely atrophied. The other nerve bundles were normal; the general perineurium of the nerve formed a capsule for the tumour.

The two cases which follow, are reported by Dr George H. Hume, of Newcastle-on-Tyne.

Fibro-sarcoma of the left sciatic nerve: excised along with a portion of the nerve: patient lost sight of.

A man aged twenty-four had noticed a lump in the back of his thigh for five months. There was a good deal of pain below the knee and in the foot, so aggravated at night as to prevent sleep. There was no impairment of motion or loss of sensibility. The tumour was easily shelled out, and was removed along with the nerve from just below the buttock to the upper part of the ham (in all six inches of the nerve). The nerve was distinctly thickened above and below the tumour, as if it were infiltrated with the tissue of the tumour. The wound healed rapidly, and in a month the patient was able to walk about without any support. When seen six months later, the foot had a smooth blue aspect, the limb was sensibly colder than the other, and was a good deal wasted. There were two small trophic ulcers on the outer border of the foot. In spite of the complete paralysis of all the muscles below the knee, his gait was astonishingly firm. The ability to walk depended entirely on the extensors of the knee, the limb below the knee playing the part of a mechanical support. There was loss of sensibility below the knee except along the back of the leg, and on the inner side of the leg and foot. The subsequent history of the patient is unknown.

Small round-celled sarcoma of internal popliteal nerve: excision along with three and a half inches of the nerve: complete recovery of motion and sensation.

A miner, aged forty, had, for a period of four months, noticed occasional shooting pains down the outer side of the right leg while at work, especially on forcibly bending or stretching the

knee. He discovered a lump in the popliteal space a few weeks ago. Pressure on the tumour caused shooting pains down the leg. At the operation, the tumour was found to be a sarcoma growing from the internal popliteal nerve; the explanation of the pain shooting down the outer side of the leg was found to be that the short saphenous nerve was tightly stretched over the tumour. The length of the internal popliteal nerve removed with the tumour amounted to three and a half inches. The wound healed, and the man returned to work. He was able to extend the foot at the ankle by the gastrocnemius, innervated from the internal popliteal above the point of division at the operation. He walked with a slight limp. There were several large blood spaces in the tumour. The patient was seen again five years later; the motor and sensory functions had entirely recovered.

Fibro-sarcoma of digital branch of the internal plantar nerve: Chopart's amputation: local recurrence: amputation of leg: death from metastases in lungs.

Herczel reports the case of a lady aged twenty-eight, who had suffered for ten months from severe pains in the right great toe; eight months later there was some swelling. Professor Czerny diagnosed a periosteal sarcoma involving the plantar nerve, and amputated through the mid-tarsal joint. The tumour was found to originate in the first digital branch of the internal plantar nerve, the latter being fusiformly enlarged at a distance of 4 cm. from its entrance into the tumour, and also where it leaves the tumour. Microscopical examination showed it to be a fibro-sarcoma, here and there undergoing myxomatus degeneration, causing extensive disappearance of the nerve fibres.

A few months after the mid-tarsal amputation there were evidences of recurrence, and the limb was removed at the upper

third of the leg; although the amputation was performed through healthy tissues, the patient died of secondary growths in the lungs less than a year from the first operation.

Myxo-fibroma of left sciatic nerve: excision of tumour along with five inches of the nerve: local recurrence as spindle-celled sarcoma, and death from internal metastases.

Dr Sydney Coupland reported this case for Dr Daniel Balding at the Pathological Society of London. A farm labourer, aged thirty-four, had for three years complained of pain in the left leg, and one year before he noticed a swelling on the back of the thigh about three inches above the knee. The tumour was not very tender, but the pains in the leg prevented him from working.

It was removed along with five inches of the nerve. The tumour measured three inches long by one and a half inches wide, and was enclosed in an ill-defined fibrous capsule, continuous at either end with the sheath of the sciatic nerve. A few fibres of the nerve were spread over the surface of the tumour; the greater number were collected into one large bundle. It was considered to be a fibro-myxoma.

The condition of the limb six months after the operation was as follows:—the knee is semi-flexed, but movement of the joint is preserved; there is no movement at the ankle; the foot is inverted, and the toes pointed; the muscles of the leg are wasted; walking (with crutches) produces œdema of the leg and lower third of the thigh. There is loss of sensibility on the back of the leg and sole of the foot.

At this time, *i.e.* six months after the operation, there were already signs of local recurrence; a tumour formed and gradually increased in size. He died within two years of secondary growths in the left pleura and posterior mediastinum. The recurrent tumour

in the thigh occupied the lower six inches of the divided sciatic nerve, the fibres of which are spread out over the upper part of the growth. The external popliteal nerve presented a fusiform swelling or tumour, one and a half inches below the cut end of the nerve, the swelling being an inch in length. The recurrent and secondary growths were of the type of a spindle-celled sarcoma.

Fibro-sarcoma of the right median nerve in the upper arm: excision of the tumour along with a portion of the nerve and of the brachial artery: gangrene of arm: amputation.

Dr Kriege of Strassburg, records the case of a girl aged nineteen, who had noticed, six months before, a tumour at the lower part of the right axilla. It grew rapidly to the size of a man's fist, and was then excised. At the operation, it was found to involve the median nerve, and to be so adherent to the brachial artery that the latter vessel had to be ligatured. This was followed by gangrene of the arm, necessitating amputation at the shoulder. One half of the tumour was surrounded by the separated bundles of the median nerve. There were several large cystic cavities in the interior of the growth, which was found on microscopical examination to be a spindle-celled fibro-sarcoma. A very small number of completely dissociated, and partially degenerated nerve fibres were seen running through the tumour substance.

Spindle-celled sarcoma of the right sciatic nerve: excision: recurrence: nine operations altogether: death from metastases.

Finotti records the case of a man aged twenty-six, who had noticed, one year before, a painful tumour in the back of the right thigh about the size of an egg. Motion and sensation were normal.

The tumour was shelled out from the sheath of the nerve and found to be a spindle-celled sarcoma, originating in the endoneurium. Three months later a second operation was required for recurrence of the growth; in order to remove it, six inches of the nerve had to be sacrificed. Altogether, nine operations were performed, each one more difficult than the preceding, the patient ultimately dying of metastases, a little more than three years after the original operation.

Sarcoma of the external popliteal nerve: excision of the tumour along with a portion of the nerve.

Dr A. G. Gerster of New York, records the case of a man aged fifty, who, after a history of three years of pain in the right thigh and leg, with the gradual development of a small tumour in the popliteal space, had come under his care in September 1894. The tumour was the size of an English walnut, and was very tender on pressure, the pain shooting down to the foot. The peroneal muscles were atrophied and presented the reaction of degeneration. Sensibility to touch and temperature were only slightly diminished. The tumour was removed along with a portion of the nerve, the fibres of the latter passing directly through the former. The ends of the nerve were stitched together. No return of function was noted when the patient was exhibited three weeks later.

Rapidly growing tumour (sarcoma?) of the Gasserian ganglion: excruciating neuralgia: death.

THIS CASE IS RECORDED BY R. W. SMITH.

"In the year 1836, an emaciated and unhealthy-looking female, about forty years of age, was admitted into the Richmond Hospital, under the care of Dr Hutton, complaining of neuralgia of the right

side of the face. She stated that the pain had commenced several months previously, had gradually increased in severity, and had now become almost insupportable; she had lost flesh, her sleep was broken, and her appetite had failed. Her countenance indicated extreme suffering; the pain (which, although subject to exacerbations, never altogether ceased), was accurately limited to the right side of the face and forehead, and when indicating the situations in which it was most severe, the patient marked with her finger the course of the branches of the fifth nerve, and more especially the point of exit of the superior maxillary from the infra-orbital foramen. Her sufferings were so much increased by mastication that she ate but little, and speaking aggravated the pain to such a degree, that she always remained silent, unless when interrogated, and even upon these occasions she frequently replied by signs. She had no respite from suffering during the day, and at night sleep seldom came to her relief, nor did any of the numerous remedies employed succeed in affording even temporary ease. After having endured more severe and more uninterrupted pain than I had ever witnessed in any other instance, death terminated her protracted agonies, four months subsequent to her admission into the hospital.

"*Autopsy.*—When the cranium was opened and the brain removed, a tumour was seen in the right division of the spheno-temporal fossa; it was somewhat of the form and size of a walnut, and occupied the position of the Gasserian ganglion; it extended across the inner extremity of the great wing of the sphenoid bone, as far forwards as the foramen lacerum orbitale, and was covered by the superficial lamina of the dura mater, which was attenuated to a remarkable degree. The trunk of the fifth nerve appeared to enter the posterior part of the tumour; the interior of which, however, presented no trace of nervous structure; the ophthalmic division crossed the anterior part of its superior surface; the superior maxillary emerged from it at the foramen rotundum; and the third

division seemed to be identified with a remarkable prolongation of the tumour, which passed through the foramen ovale, the circumference of which was increased to more than double its natural extent."

"The surface of the petrous portion of the temporal bone, which supported the posterior part of the tumour, was absorbed, as well as the superior wall of the horizontal portion of the carotid canal; between this rough and denuded portion of the bone and the deep surface of the tumour ran the Vidian nerve, which throughout its whole course was much larger than natural. The tumour was solid and of uniform consistence; its section exhibited a cellular structure, without any trace of nervous tissue; nerve fibres could, however, by the assistance of the microscope, be seen upon various parts of its surface. The non-ganglionic portion of the nerve was compressed, but not enlarged."

CHAPTER IV

DIFFUSE OR GENERALISED NEURO-FIBROMATOSIS

(v. Recklinghausen's Disease)

ELEPHANTIASIS NERVORUM (Bruns)

In contrast to the solitary tumours of nerves, the pathological and clinical status of which has been defined in the preceding chapters, we find considerable difficulty in defining the diffuse connective-tissue overgrowths related to nerves, for these embrace a number of lesions, affecting the skin as well as the nervous system, which are capable of assuming very different forms, of occurring in combination or independently of each other, and which, although presenting many analogies with tumours, are to be regarded as being rather of the nature of hypertrophies and hyperplasias.

By far the best known members of this complicated group are the so-called multiple neuromata, which were long regarded as multiple independent tumours of nerves, and as being analogous to multiple tumours of bone or of fat. Further observation has shown that what appear to be independent tumours are really local exaggerations of a diffuse or generalised overgrowth of the connective tissue sheaths of the nerves (neuro-fibromatosis), so that they can no longer be regarded as tumours in the strict sense of the term.

The less well-known and very characteristic plexiform neuroma has likewise lost its independence, and must be included in this group, for it has been shown to be the result of a localised fibro-

matosis following the distribution of a particular nerve or nerve plexus; its etiological, structural and pathological relationships are very similar to the generalised form of the disease.

What has been called by Garré, "secondary malignant neuroma," necessarily belongs to this group, because it is the result of the sarcomatous transformation of one or other of the preceding types.

The limits of the group have been further extended by the inclusion of certain lesions of the skin, the connection of which with the nervous system had for a long time remained unsuspected. The most important addition under this head is the *Molluscum Fibrosum*, or skin fibroma, the nerve origin of which was demonstrated by von Recklinghausen in 1882; his observations showed that the molluscum fibrosum was essentially a fibromatosis of the terminal filaments of the cutaneous nerves, and that it was frequently associated in the same individual with connective tissue overgrowths of the trunks of nerves.

From the more exuberant forms of molluscum fibrosum, it was an easy step to recognise the nerve origin of certain forms of *Elephantiasis*, and especially those of congenital origin, which are to be regarded as a more extensive and uniform overgrowth of tissue of one or other part or segment of the body, occurring independently, or in association with plexiform neuroma, or with the more generalised fibromatosis of the nerve trunks.

The occurrence of excessive pigmentation of the skin, not only in relation to cutaneous tumours, and to elephantiasis, but in association also with the generalised disease in the trunks of nerves, has still further added to the list of morbid conditions included in the group at present under consideration; these may be arranged in tabular form as follows :—

1. Multiple neuro-fibromata—Generalised neuro-fibromatosis.
2. Plexiform neuro-fibroma—Plexiform neuro-fibromatosis.
3. Molluscum fibrosum—Cutaneous neuro-fibromatosis.

4. Elephantiasis neuromatosa.
5. Pigmentations of the skin associated with neuro-fibromatosis.
6. "Secondary malignant neuroma," being the sarcomatous transformation of one or other form of neuro-fibromatosis.

The difficulty of giving a systematic description of these lesions is much increased by the fact that they may occur independently of each other, or in every possible combination, and that they overlap and run insensibly into one another. There is not even a good general name for the group which will include all its members, unless we adopt that suggested by certain French authors, viz.—"von Recklinghausen's Disease," or that suggested by Bruns, "Elephantiasis Nervorum." We shall describe the individual lesions separately in the first instance.

I.—GENERALISED NEURO-FIBROMATOSIS. MULTIPLE NEURO-FIBROMATA

The clinical and post-mortem records of this remarkable disease are so numerous and so exhaustive, that there is no want of material upon which to base our description. The bibliography of multiple neuroma is truly an *embarras de richesses*. There is general agreement among authors regarding the main points of the disease; discussion has long waged, however, concerning the behaviour and fate of the nerve fibres, and concerning the origin and nature of the lesion.

The pathological anatomy of the generalised neuro-fibromatosis may be considered under the following heads:—

1. The external characters of the affected nerve trunks and ganglia.
2. The changes observed in transverse and longitudinal sections of the nerves.
3. The structure and the seat of the fibromatosis.
4. The changes in the nerve fibres involved by the fibromatosis.

5. The distribution of the fibromatosis in the cerebro-spinal nerves.
6. Intramuscular fibromatosis.
7. Cutaneous fibromatosis.
8. The fibromatosis in the sympathetic nerves and ganglia

Pathological Anatomy

The external characters of the affected nerve trunks and ganglia.

These have been very fully described and illustrated in R. W. Smith's famous Memoir,[1] from which one of the accompanying figures has been copied. The nerves are not only the seat of the most remarkable multiplicity of apparent tumours, but are diffusely and unequally thickened—it may be throughout their whole course, from their origin in the brain or spinal cord to their terminations in muscle and in skin, or it may be only at points along their course. So far as the tumours are concerned, they resemble in many respects the true circumscribed tumours of nerve trunks described in the preceding chapter. They vary in size from the most minute elliptical thickenings of the nerves, up to tumour masses measuring a foot in length, and a foot and a half in circumference. They are oval, elliptical, or spherical in shape. They are encapsulated by the external sheath of the nerve trunk to which they belong. They may be loosely held within their capsule, and shell out readily when the latter is divided, or they may be more or less adherent, so that portions of the tumour tissue are liable to be left behind on attempting to enucleate the tumour from its capsule.

[1] Smith's preparations are now in the possession of the Royal University of Ireland. Through the kindness of Sir James Meredith, the secretary, and Dr Adeney, the curator, I was enabled to examine Smith's preparations and casts on the occasion of a recent visit to Dublin.

PLATE II.



Tumour of left great sciatic nerve (length, 11 inches; breadth, 10 inches).
From one of R. W. SMITH's cases of generalised neuro-fibromatosis.)

PLATE III.



The left great and small sciatic nerves from one of the author's cases of generalised neuro-fibromatosis.

The transverse section of the great sciatic nerve measures 2·5 × 1·5 em. ; its external surface presents a series of elliptical bulgings. The small sciatic nerve is thickened and beaded.

PLATE IV.



The right anterior crural nerve and its branches from one of the author's cases of generalised neuro-fibromatosis.

Portions of the extensor and adductor muscles have been retained in the dissection to illustrate the fibromatosis of the nerve filaments within the muscles.

Externally, the capsule may be smooth and glistening, and only loosely connected by areolar tissue to the adjacent structures, or it may be matted to these by new fibrous tissue, more especially after exposure to injury and pressure, or when they have rapidly increased in size. The relation of the "tumour" to the nerve fibres of the affected nerve trunk varies, just as in the solitary and circumscribed tumours; they may be spread out more or less uniformly all over the "tumour," or upon one of its aspects, or they may pursue their course over the "tumour" without any appreciable dispersion of the bundles from one another. The bundles of nerve fibres may be visible through the capsule, or the latter may require to be removed in order to trace them; whether dissociated from each other or not, they exhibit in their course over the "tumour," independent spindle-shaped thickenings which are most characteristic (Plate II.), and which serve to differentiate the disease from the solitary and circumscribed tumours of nerves.

The substance of the tumours is usually firm, or soft solid, greyish-white, but little vascular, often glistening or translucent; towards the periphery they may be more fibrous and fasciculated in appearance, while towards the centre they may present yellow areas, or points of brown pigmentation from hæmorrhage, or areas of gelatinous softening, or cysts. There may be one large cyst, or a number of smaller ones. The number of tumours and their relations to one another varies indefinitely; there may be one tumour on a nerve trunk, or several hundred; and these may succeed each other in the course of a nerve so closely that the latter appears like a string of beads.

In addition to what have been described as "tumours," the nerve trunks may be thickened so that they attain twice or three times their normal dimensions; hence it is that a minute nerve affected with fibromatosis may be actually more bulky than a large nerve

trunk, such as the great sciatic or musculo-spiral. The original size of the nerve affected can only be gauged by counting the bundles of nerve fibres seen in a transverse section.

The thickening of the nerve trunk rarely appears as a uniform increase in its girth; the external surface presents rather a series of localised elliptical bulgings or projections, corresponding to localised thickenings of individual nerve bundles at the periphery of the nerve trunk, or of those more centrally placed.

There are all transition stages between what may be called a thickening of a nerve, and what may be called a tumour.

The thickening of the nerve trunks, and the appearance of tumours, are alike due to an overgrowth of the connective tissue elements of the sheaths of the nerves; this is best studied in series of transverse and longitudinal sections of the nerves affected, with the assistance of the differential stain of Weigert or its modifications.

Ganglionic enlargements of nerves.—The only ganglia of the cerebro-spinal nerves commonly involved in neuro-fibromatosis are those on the posterior roots of the spinal nerves; they undergo an enlargement or thickening similar to that of the nerve trunks; they may attain the size of hazel-nuts, and their enlargement may be attended with a corresponding increase in the size of the inter-vertebral foramina. The changes in the ganglia of the sympathetic system are described later.

In transverse sections of an affected nerve trunk, examined under a low magnifying power, the most important change is seen to be the formation of new connective tissue (fibromatosis) within the primary bundles of nerve fibres. The distribution of the fibromatosis within any given nerve trunk is subject to infinite variations; some bundles escape altogether, others are only affected to a slight degree, others again are very markedly affected (Plate V.). Certain bundles are affected at one level, and are exempt at another. Central and peripheral bundles are picked out quite impartially.

PLATE V.



Transverse section of the right median nerve from one of the author's cases of generalised neuro-fibromatosis.

Weigert-Pal. *Leitz No. 3 objective.*

PLATE VI.



FIG. 1.—Transverse section of the left median nerve above level of tumour.
Weigert-Pal. Zeiss 3 *in. objective.*

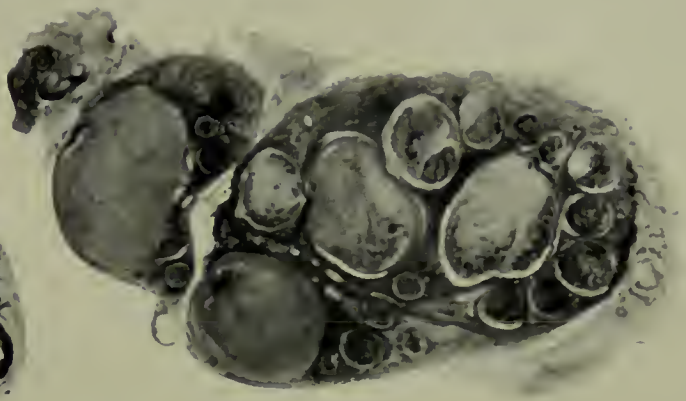


FIG. 3.—Transverse section of the left median nerve below level of tumour.
Weigert-Pal. Zeiss 3 *in. objective.*

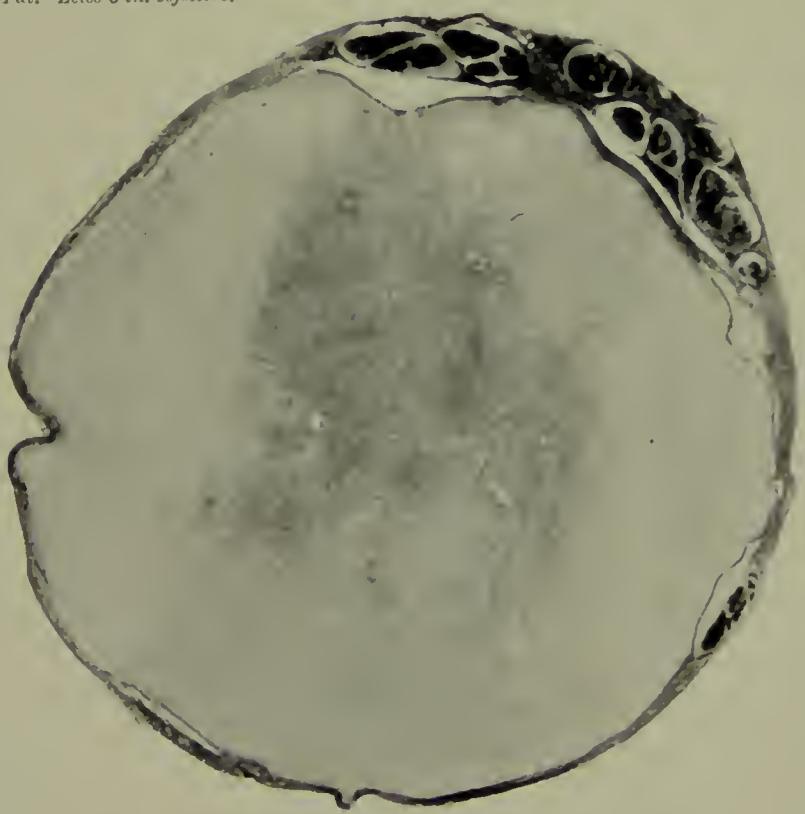


FIG. 2.—Transverse section of the left median nerve through the tumour.
Weigert-Pal. Zeiss 3 *in. objective.*

Appearances of the median nerve at different levels in the upper arm, from one of the author's cases of generalised neuro-fibromatosis.

PLATE VII.

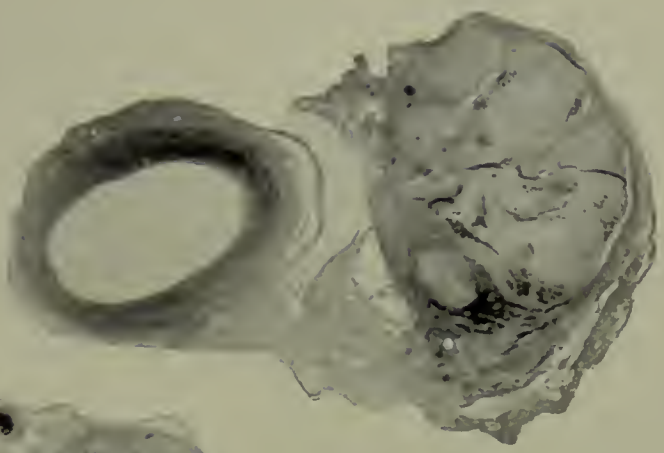


FIG. 3.—Transverse section of Vagus nerve below level of tumour, along with the carotid artery.

Weigert-Pal.
Zeiss 2 in. objective.

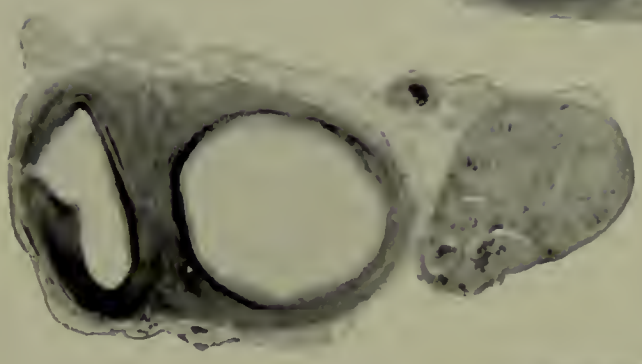


FIG. 1.—Transverse section of Vagus nerve above level of tumour, along with the carotid arteries.

Weigert-Pal.
Zeiss 3 in. objective.



FIG. 2.—Transverse section of Vagus nerve through the tumour, along with the common carotid artery.

Weigert-Pal. *Zeiss 3 in. objective.*

Appearances of the Vagus nerve at different levels in the neck, from one of the author's cases of generalised neuro-fibromatosis.

Where there are two or more groups of nerve fibres within the same perineurium, one may be exempt while the others are affected.

In certain bundles, the fibromatosis takes place between the perineurium and the enclosed fibres, either uni-laterally, or circumferentially, while in others it is distributed more uniformly, so that the individual nerve fibres come to be separated or dissociated from one another.

Plate VI. represents transverse sections of the left median nerve from the same case, above, below, and through, what was clinically a tumour of that nerve. Above the tumour the nerve is only 8 mm. in its major diameter, and all except two of the dozen or more nerve bundles, exhibit a moderate degree of fibromatosis. Through the tumour the fibromatosis is almost confined to one particular bundle, which is so enlarged that it dwarfs and displaces all the others, measuring 19 mm. in diameter. Below the tumour the distribution of the fibromatosis is again different, for while it is well marked in some half dozen of the bundles, the remainder are unaffected. The magnification in all three figures being the same, they demonstrate very well that the apparent tumours in multiple neuro-fibromata are merely localised exaggerations of a fibromatosis diffused along the nerves.

In the cranial nerves, the changes are precisely the same. Plate VII. represents transverse sections of the vagus nerve (from the same case) above, through, and below a "tumour," which in the fresh state measured 2 cm. in diameter. In sections through the tumour eight nerve bundles are seen, four of which present a moderate degree of fibromatosis, while the remaining four are so enlarged that they constitute almost the entire bulk of the tumour. In sections above the tumour the nerve measures 6 mm. in its major diameter, and all the bundles of which it is composed exhibit a moderate degree of fibromatosis. Below the tumour the nerve measures 10 mm. in its major diameter, and all the bundles are affected.

In longitudinal sections of the nerve trunks the appearances are

equally eharaeteristie. Whereas in a normal nerve trunk all the nerve fibres are elosely paeked, pursue a straight course, and run parallel with one another (Plate VIII.), in neuro-fibromatosis the individual fibres tend to beeome separated or dissoeiated by the formation of new eonneetive tissue between them, and they pursue a wavy or spiral eourse, diverging eonsiderably from the longitudinal axis of the nerve, so that it is diffieult to traee individual nerve fibres for any distanee (Plates VIII. and IX.). The nerve fibres are lengthened in proportion to the degree of dissoeiation and eonsequent deviation from their original eourse.

The structure and seat of the fibromatosis.

There is general agreement that the endoneurial eonnective tissue between the individual nerve fibres is the ehief seat of the pathological proeess. In a normal nerve the endoneurium is very small in amount, and very delieate in strueture; in neuro-fibromatosis it is inereased to sueh a degree as to give rise to visible thiekenings and tumours of the nerves. In thin seetions or in teased preparations, it is seen to be made up of a delieate fibrillated network separating the original fibres or lamellæ of the endoneurium; the fibrils of the network are the braneling and anastomosing proeesses of eells; the latter are, for the most part, spindle-shaped with oval nuelei, and they lie either in the spaees of the network, or grasping the endoneurial lamellæ. By some observers they have been erroneously regarded as nerve eells. In the spaees of the network there are also lymphocytes and eertain rounded eells, about twice the size of a red blood eorpusele, possessing a small round nueleus and finely granular protoplasm. The tissue as a whole is well supplied with blood-vessels, and its spaees are filled with lymph. It has been suggested by Finotti that the eells above deseribed are the result of a proliferation of the endothelial eells lining the lymphatie spaees of the endoneurium.

PLATE VIII.

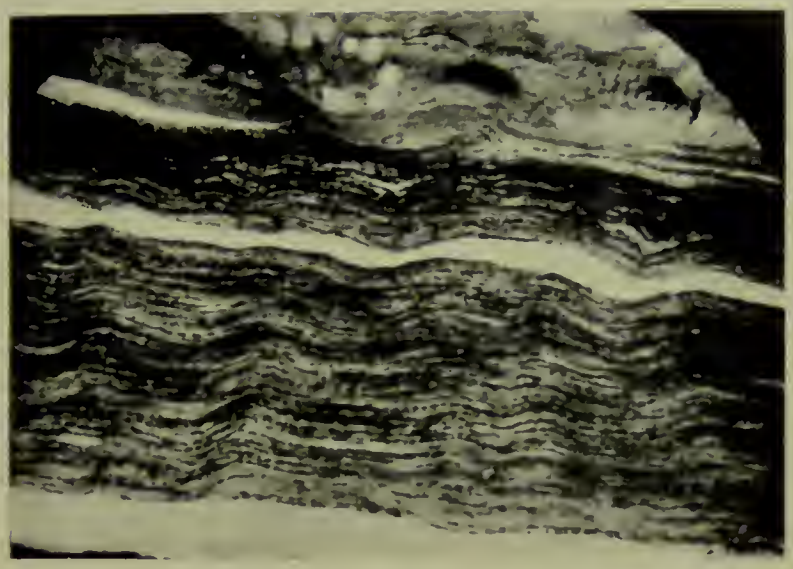


FIG. 1.—Longitudinal section of normal sciatic nerve, showing the compact and parallel arrangement of the nerve fibres.

Weigert-Pal. *Leitz No 3 objective.*

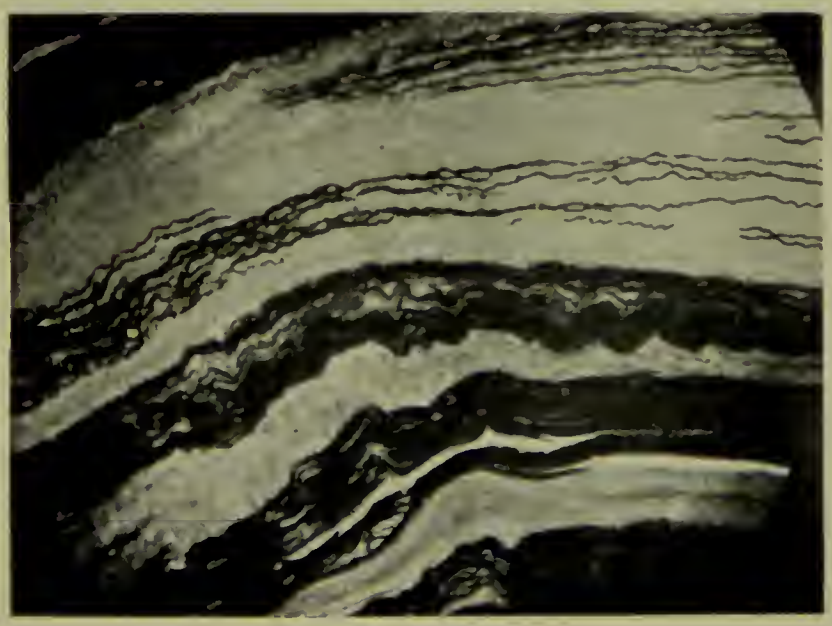


FIG. 2.—Longitudinal section of sciatic nerve in neuro-fibromatosis, showing the dissociation and wavy course of the nerve fibres.

Weigert-Pal. *Leitz No. 3 objective.*

PLATE IX.

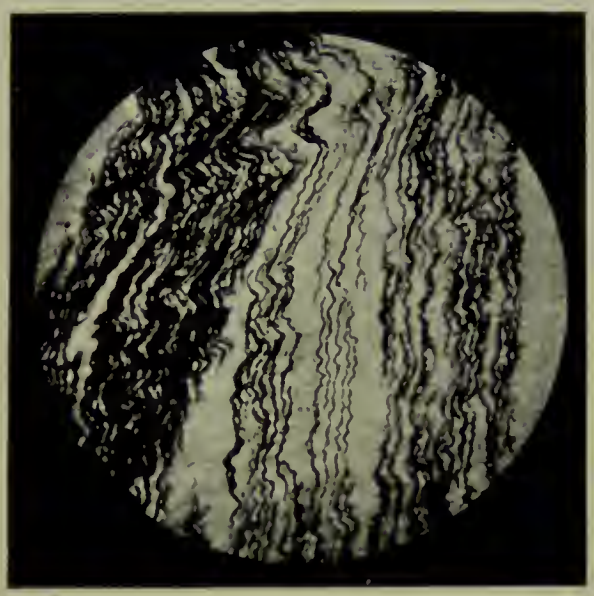


FIG. 1.—Longitudinal section of sciatic nerve in neuro-fibromatosis.
Weigert-Pal. *Leitz No. 3 objective.*

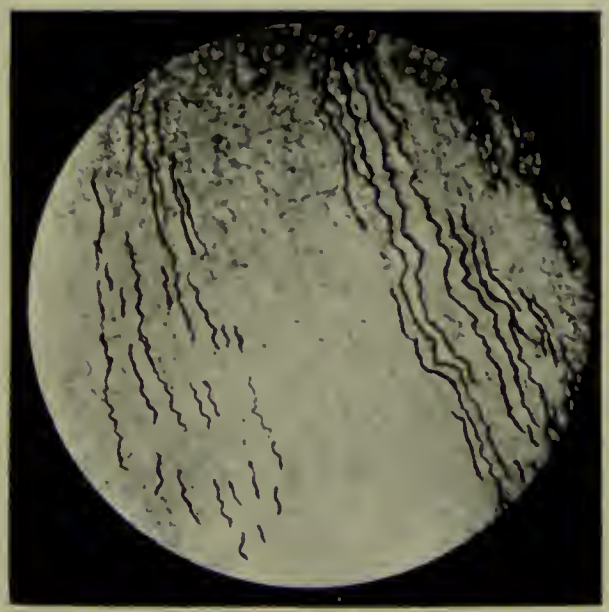


FIG. 2.—Longitudinal section of sciatic nerve in neuro-fibromatosis.
Weigert-Pal. *Leitz No. 3 objective.*

There is a gradual transition between the overgrown endoneurium and the definitely lamellated perineurium surrounding it.

The overgrown endoneurium does not resemble the tissue of any new growth. Its characters are remarkably constant in different cases of the disease, in different nerves from the same case, and at different stages in the progress of the same case. It may vary a little in the different nerves to the extent of being looser, more open, and more cellular in one nerve, and firmer, more compact, and more fibrous in another, depending probably on the duration of the lesion in the particular nerve, and on the rapidity with which the new tissue has been formed.

In one of the author's cases, the tissue was looser and more cellular in the vagus, which was observed to become enlarged two years before the patient's death, than in the median nerve, which had been enlarged for at least six years. At the same time the fibromatosis of the endoneurium does not appear to be a progressive lesion in the same sense as the common forms of chronic interstitial inflammation or cirrhosis.

The occasional variations in the size, prominence, and tension of the tumours observed clinically in cases of multiple neuro-fibromata, would appear to correspond to variations in the amount of lymph in the meshwork of the tissue composing them, and it may be also to variations in the amount of blood in the vessels.

The *perineurium* usually remains unchanged ; Finotti and others have observed, however, the perineurium to participate in the fibromatosis, this being attended by an increase in the number of its concentric lamellæ. The perineurium is not so well defined in the cranial as in the spinal nerves.

The *epineurium* or general sheath of the nerve normally consists of a loose areolar tissue, with clumps of large fat cells and numerous blood-vessels. In neuro-fibromatosis it is more compactly arranged and increased in amount ; the blood-vessels are much larger and

more numerous. The fat cells may largely disappear; in the author's experience this is more marked in nerves removed post-mortem than in those removed by operation at an earlier stage of the disease.

The effects of the fibromatosis on the nerve fibres.

The behaviour of the nerve fibres is one of the most disputed points in the morbid anatomy of neuro-fibromatosis, and although the subject has received great attention, and although the most modern methods of staining the nerve fibres have been employed for its elucidation, it still remains undecided whether the nerve fibres participate in the morbid process, or whether they remain passive and unaffected by the changes surrounding them.

That the nerve fibres are lengthened as they pass over the tumour-like enlargements of the nerves, or where they are dissociated from one another by the formation of new connective tissue between them, so that they pursue a wavy or spiral course, has already been referred to. Several observers have maintained that new nerve fibres are formed, firstly of the non-medullated variety with a subsequent conversion of these into medullated fibres by the acquisition of a white sheath. Although it is difficult to prove the negative, the new formation of nerve fibres may be regarded as unlikely in the absence of nerve cells.

There is greater difficulty in deciding the question as to the occurrence of degeneration in the already existing nerve fibres. The observers who maintain that there are no changes in the fibres beyond their mechanical displacement, include von Recklinghausen, Lahmann, Kriege, Westphalen, Strube, and Goldmann. Those who believe in the occurrence of degeneration include Marchand, Pomorski, Hürthle, Jordan, Kyrileis, Herczel, and von Winiwarter.

In the examinations of preparations of nerve fibres, there are certain sources of fallacy apart from post-mortem changes, arising from faulty preparation, and imperfect staining by Weigert's or other methods. The appearances observed in longitudinal sections are liable to be misinterpreted ; the dissociated nerve fibres pursue such a tortuous course that it is difficult to trace any individual fibre, while the partial, interrupted views are apt to give an appearance of segmentation and degeneration of the medullary sheath. It is not easy, therefore, to absolutely demonstrate degenerative changes. The author hoped that by examining a series of transverse sections, above, through, and below a visible tumour of a nerve trunk which was likely to exert injurious pressure on the nerve fibres, and by comparing the appearances at the different levels, some definite evidence would have been obtained ; this method of observation, however, has not yielded the results anticipated.

The author believes, however, that he has observed degenerative changes in two cases of multiple neuro-fibromata, in which the point in question was specially investigated ; there was evidence of segmentation, disintegration, and disappearance of the myeline sheath ; it was also suggestive that in transverse sections of nerve bundles, in which the fibres were completely dissociated from one another, and entirely surrounded by the overgrown endoneurium, they either did not stain at all, or very imperfectly, and this in spite of the most careful and prolonged staining by Weigert and Pal's methods, whereas in the fibres of adjacent bundles, which had not been dissociated, the medullary sheaths stained most satisfactorily.

That there was no degeneration of the nerve fibres in the cases investigated by Goldmann and others, does not prove its absence in other cases. The author is of opinion that degeneration of the nerve fibres may occur in cases of generalised neuro-fibromatosis,

but that it is exceptional, and of comparatively little importance. It is very different in the case of sarcomatous transformation of the overgrown endoneurium, this being followed by the most extensive degeneration and destruction of the nerve fibres similar to that already described as occurring in the primary sarcoma of nerves.

In the case of the optic nerve, it is comparatively common to have degeneration of the nerve fibres and amaurosis, although the "tumour" of the nerve may be innocent. Goldmann maintains that the atrophy is not the result of pressure on the nerve fibres, but is due to the interference with the circulation, causing neuro-retinitis and subsequent atrophy.

Distribution of the fibromatosis in the cerebro-spinal nerves and ganglia.

Nothing is more striking in the morbid anatomy of neuro-fibromatosis, than the variations in its distribution throughout the peripheral nervous system. It varies so indefinitely, that scarcely any two recorded cases are alike. It may pick out certain peripheral nerves, or nerve plexuses, or it may specially select the cranial nerves, or the spinal nerves, or it may be scattered irregularly here and there throughout the body, or again it may be generalised so that scarcely a single nerve escapes. Sometimes the thickening of the nerves is the more prominent feature; at other times, the tumour-like enlargements, but more often, there is an unequal combination of the two.

As erroneous statements have been made regarding the distribution of the lesion, from the time of Rokitansky down to the present day, I have collected the reports of forty-five cases in which a complete post-mortem examination was made, which give more accurate information as to the distribution of the lesion, than the

records of clinical cases in which the more prominent tumours observed during life are alone indicated.

The cranial nerves are affected in about two-thirds of the recorded cases. No single cranial nerve is exempt, although the reverse has been affirmed of the olfactory, optic, and auditory. Some are affected much more commonly than others; this is made evident in the following table, showing the order of frequency :—

Vagus	in 29 cases
Trigeminal . . .	,, 12 ,,
Hypoglossal . . .	,, 7 ,,
Portio dura . . .	,, 6 ,,
Spinal Accessory . .	,, 6 ,,
Oculo-motor . . .	,, 6 ,,
Glosso-pharyngeal . .	,, 4 ,,
Optic	,, 4 ,,
Auditory . . .	,, 3 ,,
Abducens . . .	,, 3 ,,
Trochlear . . .	,, 3 ,,
Olfactory . . .	,, 1 case.

Sometimes only one nerve is affected, *e.g.* the vagus, or trigeminal; sometimes a large number (in Gerhardt's case as many as nine) are simultaneously diseased. They may present a normal appearance until they emerge from the skull; the vagus in the neck may be as thick as a finger, or may resemble a string of hazel-nuts; the hypoglossal may present as many as twenty tumour-like enlargements in the course of its peripheral distribution. Less frequently they are involved before they leave the skull, it may be within the dura, and close up to their origin from the brain.

In the vicinity of the bony foramina, the enlargement of the nerve may result in a widening of the aperture in the bone; in the vicinity of the brain, they may press upon and give rise to

hollows in the cerebellum, pons, etc., with symptoms of cerebral or cerebellar tumour. In the case of the optic and auditory nerves, there may be atrophy of the nerve fibres, and consequent blindness or loss of hearing. Enlargement of the spinal accessory as it passes through the foramen magnum, may press upon the medulla oblongata. The ganglia related to the cranial nerves are very rarely involved; in Nélaton's clinique, a case was observed in which both the ophthalmic and Gasserian ganglia were very voluminous. Generisch also records a case in which the ophthalmic ganglion was enlarged.

The spinal and peripheral nerves would appear to be invariably affected. Thickening and tumour-like enlargements of the spinal nerves within the spinal canal are met with in about one fourth of the recorded cases, so that pressure on the spinal cord is comparatively common in neuro-fibromatosis. In a small number of cases (three) the nerve roots were affected close up to their origin from the cord, both anterior and posterior roots, or either alone. More frequently the spinal nerves are not affected until after their emergence from the dura, or from the intervertebral foramina. The ganglia on the posterior roots are not infrequently enlarged, so that they attain the size of hazel-nuts. The intervertebral foramina are then correspondingly widened to accommodate them.

Within the spinal canal the neuro-fibromatosis is more commonly observed and is more pronounced in the region of the cauda equina and in the cervical region, or it may be more generally and quite irregularly distributed up and down the spinal canal.

Beyond the points of emergence of the nerves from the intervertebral foramina, the disease may be local or general, as already indicated.

One or other of the great nerve plexuses (cervical, brachial, lumbar, sacral) is not infrequently the chief seat of the disease.

The intercostal nerves have been specially selected in certain

cases, it may be in the form of large tumours which may press injuriously on the contents of the thorax, or their terminal branches in the abdominal wall may be the seat of innumerable small subcutaneous tumours.

The nerves of the extremities are so commonly affected that the disease is usually recognised by the tumour-like enlargements which they exhibit. They are not involved in any apparent order of frequency, but it may be stated generally that the median, ulnar, and internal cutaneous in the upper limb, and the sciatic, anterior crural, and popliteal nerves in the lower limb, are those most commonly selected. Tumours are rarely met with in the distal extremities of the limbs, the author has only observed one case in which they were present in the nerves of the hand.

Intramuscular neuro-fibromatosis.

The presence of neuro-fibromatous nodules within the substance of the muscles in cases of multiple neuromata, did not escape the attention of the earlier observers. They were first seen by the author in an amputation of the arm for sarcoma in a patient with multiple neuromata; the cut surface of the muscles was studded with nodules of all sizes and shapes. On post-mortem examination of the same case two years later, the motor nerves were found to be as much affected by the disease as any of the purely sensory nerves; both before and after entering the muscles, they presented characteristic beaded or spindle-shaped thickenings, so that it was possible to trace throughout the entire length of the muscle even those minute filaments which would otherwise have been invisible to the naked eye.

Microscopically, the lesion in the motor nerve filaments is found to be the same as in the trunks of nerves already described, the fibromatosis consisting of the same peculiar loose connective tissue

characteristic of the overgrown endoneurium. The muscle fibres themselves may be quite normal, except in the immediate vicinity of the larger neuro-fibromatous nodules, where they are flattened and compressed.

Although the muscular fibres are not directly injured by the intramuscular nodules and tumours above described, they are frequently the seat of degenerative changes. In one of the author's cases, where a large sarcoma developed in the left lumbar plexus, the extensor muscles of the thigh on the same side were found to have undergone extensive degenerative changes; many of the fibres had disappeared altogether, others were hyaline and were broken up into short segments; in the place of the fibres which had disappeared, and surrounding the remains of those which had undergone degeneration, there were accumulations of fat cells, of leucocytes, and of red blood corpuscles. Similarly, there are many cases recorded of paraplegia resulting from the pressure of tumours upon the spinal cord, in which the muscles of the lower limbs had undergone complete fatty degeneration and replacement by fat.

Cutaneous neuro-fibromatosis.

Apart from the projecting tumours of the skin (molluscum-fibrosum), which will be considered later, the skin and subcutaneous tissue throughout the body, although not visibly altered on the surface, may present extensive fibromatosis in relation to the terminal distribution of the cutaneous nerves. In sections of skin, stained with Weigert's method, the terminal nerve filaments are readily recognised by the dark blue staining of the medullary sheaths; they exhibit the same fibromatosis or overgrowth of the endoneurium as has been described in the larger nerve trunks. The tissue of the true skin is also studded with innumerable tumours or fibrous nodules related to the nerve filaments; some

of these nodules are so small as only to be recognised with the mieroscope; others may attain the size of small peas, and measure 2 to 5 mm. in diameter. They are more numerous below the level of the sweat glands; in the vicinity of the latter they are usually quite distinct from them. In addition to these circumscribed nodules, there may be a more diffuse fibromatosis of the whole skin extending from the panniculus adiposus right up to the epidermis, similarly related to the thickened nerve filaments, which may be seen traversing the newly-formed tissue in all directions.

The sympathetic nerves and ganglia.

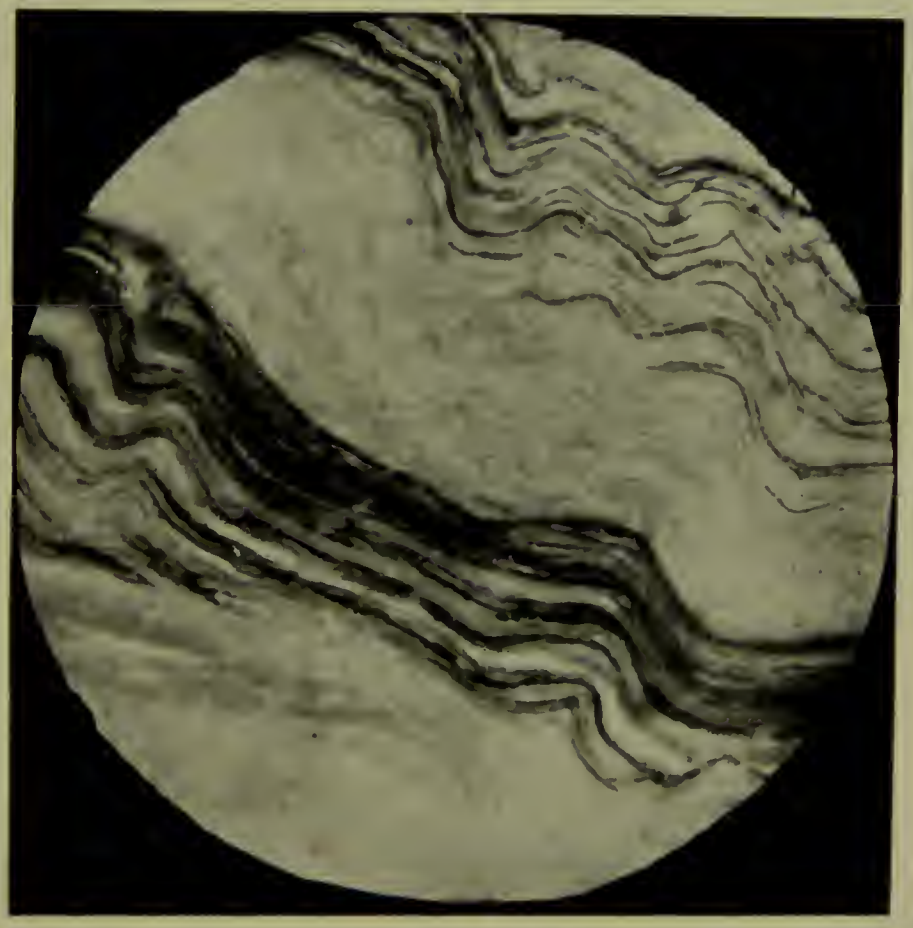
The sympathetic nervous system plays a very prominent part in the morbid anatomy of generalised neuro-fibromatosis. The early authors remarked on the great enlargement of the sympathetic nerves, and on the tumour-like masses formed in relation to the ganglia, more especially within the cavity of the abdomen. Cruveilhier, in his "Anatomie Pathologique du Corps Humain," figures a tumour-like enlargement of the accessory superior cervical ganglion.

In some of the most remarkable cases of generalised neuro-fibromatosis on record, *e.g.* those of R. W. Smith, the sympathetic system was unaffected. It is nearly always observed however in cases submitted to post-mortem examination to have participated in the disease to a degree which was entirely unsuspected during life. In one of my own cases, the fibromatosis affected the entire gangliated cord of the sympathetic and its branches of communication with the cerebro-spinal nerves, the plexuses along the carotid, aorta, and common iliac arteries, the plexus in the subserous coat of the stomach, and in the mesentery. In Gerhardt's case, the sympathetic system was much more extensively involved; there were nodules on the nerves in the stomach and pancreas, and in the bronchial plexus

extending into the interior of the lungs, there being nodules as large as a bean along the chief bronchi; the origins of the aorta and pulmonary artery were entirely surrounded by a large tumour made up of innumerable small nodules, so extensively developed on the right side as to cause absorption of the vertebræ like that resulting from the pressure of an aneurism; the splanchnics, the cœliac, mesenteric, and visceral plexuses were similarly affected; in front of the left kidney there was a tumour one-fourth larger than the kidney itself, and entering it above there was a thickened nerve cord derived from the solar plexus. In the hepatic plexus there was a large packet of nodules alongside the artery at the hilus; these could also be traced into the interior of the liver down to the smallest branches of the hepatic artery. There were similar nodules in the mesentery, intestine, neck of the bladder and seminal vesicles. In Pruddens' case all the nerves of the deep cardiac plexus were enlarged. Knoblauch describes the semilunar ganglia as being each as large as a Spanish nut. Robert Abbe describes an enlargement of the cervical sympathetic which resembled clinically a tumour of lymphatic glands.

As the result of the examination of a series of preparations, derived from the cervical gangliated cord, the gastric and hypogastric plexuses, from one of my own cases, the nature of the enlargement in the sympathetic nerves and ganglia would appear to be precisely similar to that observed in the cerebro-spinal nerves—the enlargement being due to an overgrowth of the delicate connective tissue supporting the nerve fibres and ganglion cells, *i.e.* the tissue which corresponds to the endoneurium of the cerebro-spinal nerves. The fibromatosis may be traced from the latter into the sympathetic nerve trunks and ganglia, and is met with especially in relation to the bundles of medullated nerve fibres which pass through these structures (Plate X.). The lesion was extremely well demonstrated in the minute nerve filaments derived

PLATE X.



Longitudinal section of the middle cervical sympathetic ganglion, showing the dissociation and wavy course of the bundles of medullated nerve fibres passing through the ganglion.

Weigert-Pal. *Leitz No. 3 objective.*

from the hypogastric plexus, accompanying the common iliac arteries, and contained within their sheath, and in the plexus of nerves around the external and internal carotid arteries. It was not possible to trace any nerve fibres into the arterial wall.

The overgrowth of connective tissue would appear to be more cellular than that met with in the cerebro-spinal nerves, and from the absence of a definitely lamellated perineurium surrounding the bundles of nerve fibres, it is less sharply defined from the surrounding tissues. The medullated nerve fibres exhibit the same dissociation, and pursue the same wavy tortuous course as in the cerebro-spinal nerves, and do not appear to undergo degeneration. The ganglion cells, although displaced or crowded together by the fibromatosis, do not appear to undergo any structural change; the pigmentation of their protoplasm is not any greater than that met with under normal conditions.

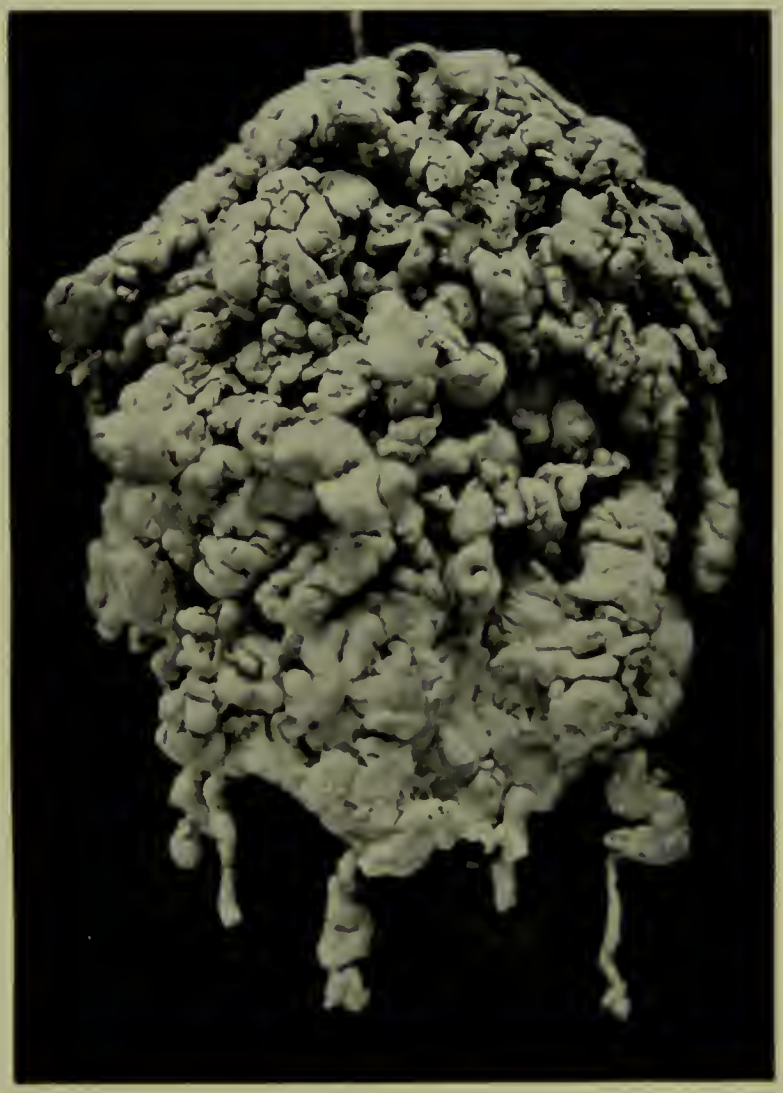
II.—THE PLEXIFORM NEURO-FIBROMA

This is quite one of the most interesting types of neuro-fibromatosis. Although specially described and named by Verneuil and by Bruns, its existence was well known to the earlier writers on neuroma. It is to be regarded as a fibromatosis confined to, and at the same time diffused throughout, the distribution of one or more contiguous nerves, or of a plexus of nerves. The nature of the lesion is essentially the same as the more generalised form of neuro-fibromatosis, and the two conditions are often met with combined in the same individual. Although decidedly rare, the number of recorded cases is already considerable; Bruns himself has collected forty-two cases; to these I am able to add eighteen from other sources, and two which have come under my own observation, making a total of sixty-two cases.

Microscopic appearances.—When removed from the body and partially dissected, the plexiform neuro-fibroma is seen to be composed of a plexus of convoluted strands or cords, held together by a soft, loose, fatty, connective tissue (Plate XI.). Bruns has likened it to a cirsoid aneurism, and proposed the name of cirsoid neuro-fibroma. It may be met with as a more or less circumscribed tumour-like mass, or it may present no capsular or other limitation; it may be met with extending throughout the greater part of the length of a limb, perforating the subjacent fascia, penetrating the substance of muscles in all directions, adherent to the periosteum, lodging in grooves or in actual gaps in bone, *e.g.* flat bones of skull, or roof of the orbit. Being most commonly situated in the subcutaneous tissue, it may be very intimately connected with the overlying skin; the latter may appear normal or pigmented, or may be enormously thickened so as to form lobulated or sausage-shaped, or complexly folded masses, the so-called elephantiasis neuromatosa or pachydermatocele.

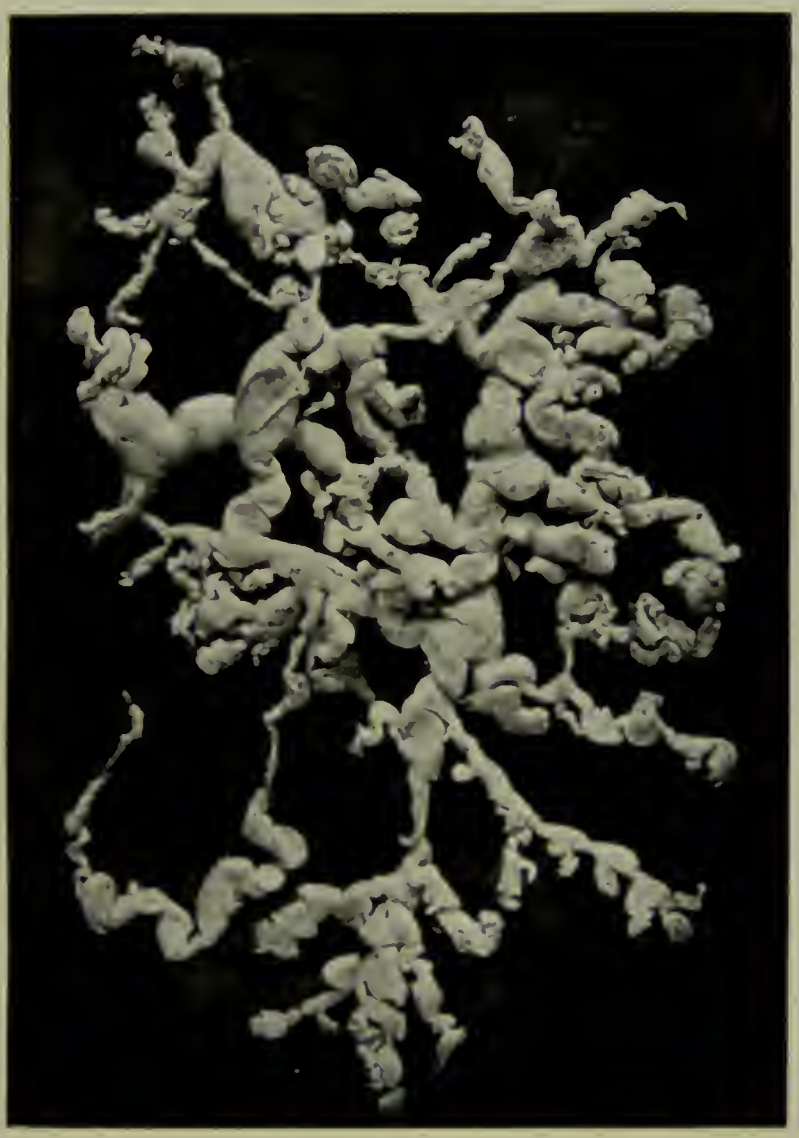
The strands of which the tumour is composed represent the thickened and elongated nerves of a circumscribed territory, usually of the skin and subcutaneous tissues. They are easily separated from each other by dissection, and may be unravelled into the irregular plexiform arrangement shown in Plate XII. They vary in thickness, quite irrespective of their proximity to their origin, from that of an adult finger down to the most attenuated filaments. They are not cylindrical, but present nodular, fusiform, or beaded swellings, not unlike grains of boiled tapioca on a string. The separated strands present a smooth shining exterior, corresponding to the perineurium of the thickened bundles of nerve fibres; the consistence of the strand is generally soft and gelatinous, without any elasticity, so that they are easily torn across. On section the tissue is greyish-white and translucent; the central portion is usually paler in colour, and tends to bulge out into the shape of a mushroom.

PLATE XI.



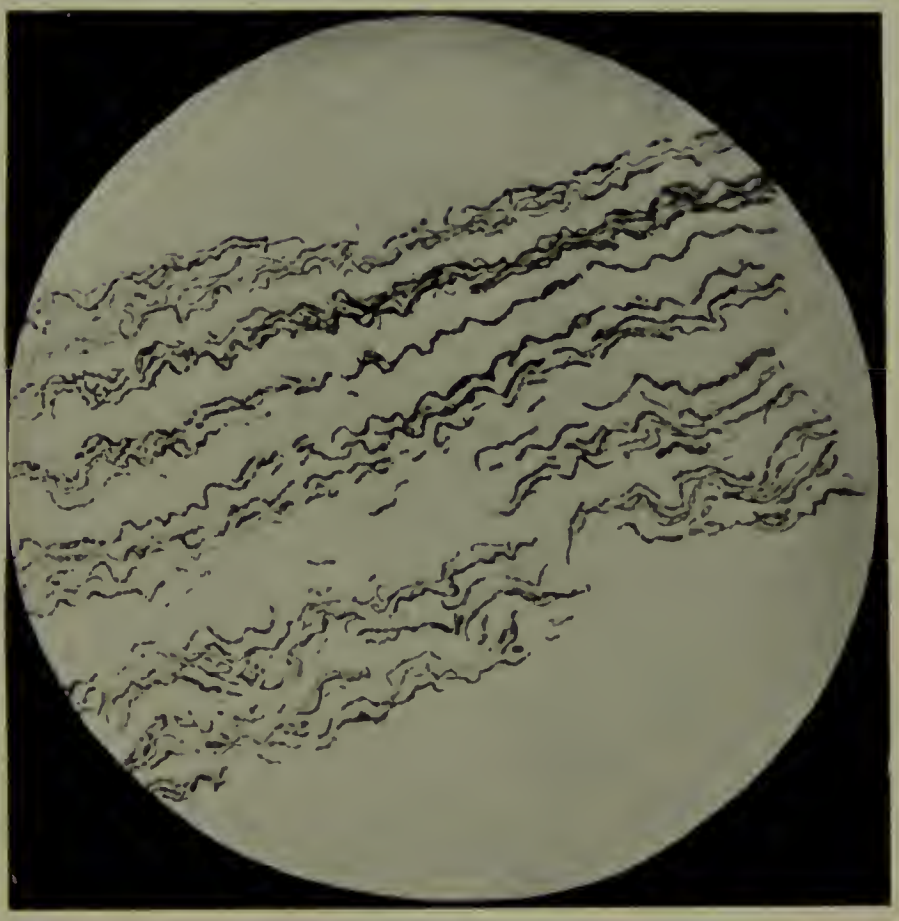
Plexiform neuro-fibroma of small sciatic nerve, excised by Prof. ANNANDALE.
Natural size.

PLATE XII.



Plexiform neuro-fibroma of median nerve in upper arm, excised by Mr J. W. B. Hodsdon.
From a dissection by Mr J. W. Dowden, F.R.C.S.Ed.

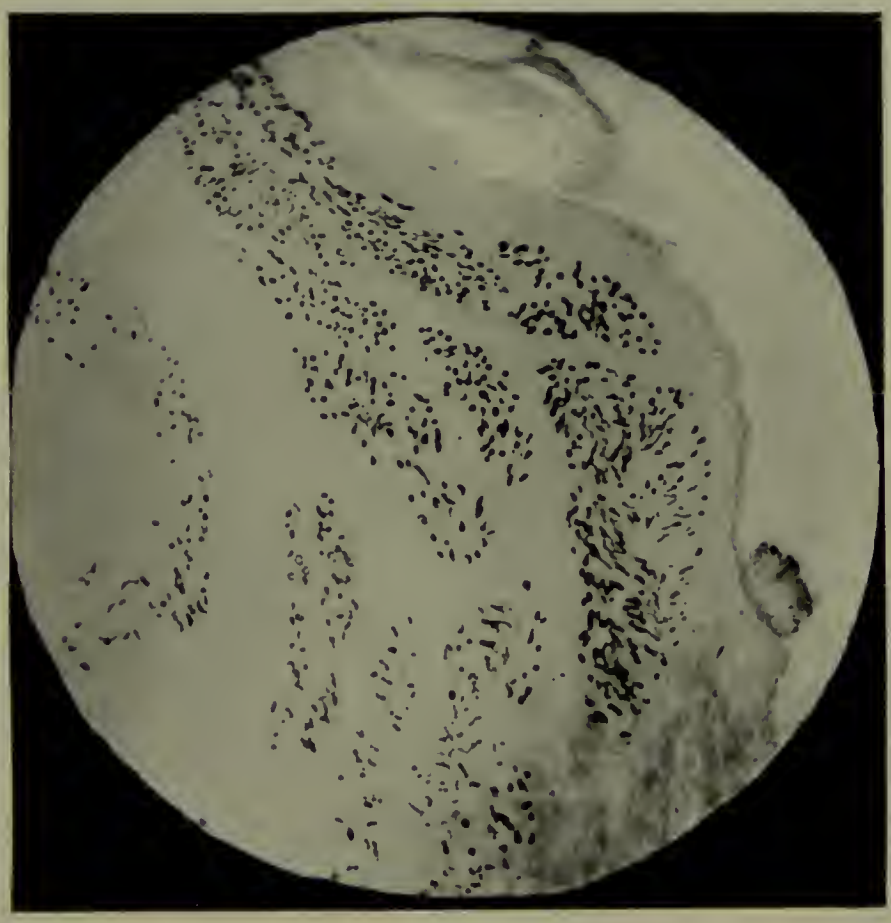
PLATE XIII.



Longitudinal section of thickened nerve strand from a plexiform neuro-fibroma, showing the dissociation and wavy course of the medullated nerve fibres.

Weigert-Pal. *Leitz No. 3 objective.*

PLATE XIV.



Transverse section of thickened nerve strand from a plexiform neuro-fibroma.

Weigert-Pal. *Leitz No. 3 objective.*

The histological characters of the plexiform neuro-fibroma were thoroughly investigated by Ziegler and Baumgarten in Bruns' specimens; their observations have been amply corroborated by Goldmann and others, and by my own preparations. The thickened nerve cords, when cut in transverse and longitudinal sections, and stained after Weigert's method, show the same overgrowth of the endoneurium surrounding, or separating the individual nerve fibres, as has been described in the generalised form of neuro-fibromatosis; the nerve fibres themselves remain passive, although they may undergo displacement and dissociation, and they may pursue a wavy or tortuous course through the thickened endoneurium. As in the generalised disease, it has been asserted that they may undergo degeneration, and may even disappear (Baumgarten), but the author is inclined to agree with Goldmann that such changes are altogether exceptional.

It is universally accepted that the pathological anatomy of the plexiform neuro-fibroma is identical with that of the generalised neuro-fibromatosis (multiple neuro-fibromata), except in its distribution and localisation. The essential lesion is the same in both. An interesting peculiarity of the plexiform type is the tendency which it may exhibit, although involving a purely sensory nerve, to penetrate adjacent muscles, and ramify in their substance. This was illustrated in one of the author's cases in which a plexiform tumour on the back of the thigh, involving the small sciatic nerve, sent prolongations of its convoluted strands through the fascia lata into the substance of the hamstring muscles. The skin and subcutaneous tissue covering a plexiform neuro-fibroma may appear normal, and yet, according to Goldmann, may present on microscopical examination, an extensive neuro-fibromatosis. All the minute nerve filaments in the pars reticularis of the cutis may be irregularly thickened, and studded with fibromatous nodules having the same structure as the strands of the plexiform tumour,

except that the perineurium of the affected nerve bundles is less defined from the surrounding connective tissue. The neuro-fibromatosis could be traced up to the pars papillaris of the cutis. The sweat and sebaceous glands, the hair follicles and blood-vessels of the skin, remain passive, and only suffer indirectly from the above changes. The skin and subcutaneous tissue in relation to a plexiform tumour very frequently present changes which are both visible and striking, and which are simply exaggerations of what has been described as seen with the microscope: the overgrowth of subcutaneous tissue and skin may reach a degree which is best described by the term elephantiasis, the skin itself frequently showing an excess of the normal pigmentation.

Anatomical situations of the plexiform neuro-fibroma.

By far the most frequent situation is the subcutaneous tissue of the head and neck in the distribution of the trigeminal and superficial cervical nerves, although it may be met with anywhere throughout the sympathetic and peripheral cerebro-spinal nervous systems. The following table includes the figures given by Bruns, with the addition of recent cases:—

Sites of plexiform neuro-fibroma.

Temple, forehead, and upper eyelid . .	18 cases.
Posterior part of neck and behind auricle .	14 ,,
Nose and cheek	4 ,,
Region of lower jaw, and anterior half of neck	5 ,,
Breast and back	8 ,,
Extremities	9 ,,

The nerves of the extremities include the median, musculo-spiral, radial, and small sciatic. Goldmann and Pomorski have each recorded a case in which the intercostal nerves were affected,

the tumour projecting into the pleural cavity. Bocasso observed a tumour below the jaw, passing along the hypoglossal nerve into the substance of the tongue.

Bruns drew special attention to the fact that the most common seats of the plexiform neuro-fibroma are also the most common situations of elephantiasis neuromatosa, or pachydermatocele, with which it is frequently associated.

Simultaneous occurrence of the plexiform with other forms of neuro-fibromatosis.

In addition to the coexistence of plexiform tumours with elephantiasis already referred to, they are also frequently associated with the generalised fibromatosis (multiple neuromata); in Bruns' series of cases this combination was present in no less than twelve, and in the twenty cases collected by the author, there was the same combination in thirteen. The coexistence of the plexiform tumour with multiple skin-fibromata (molluscum) is met with in about the same proportion of cases.

III.—CUTANEOUS NEURO-FIBROMATA

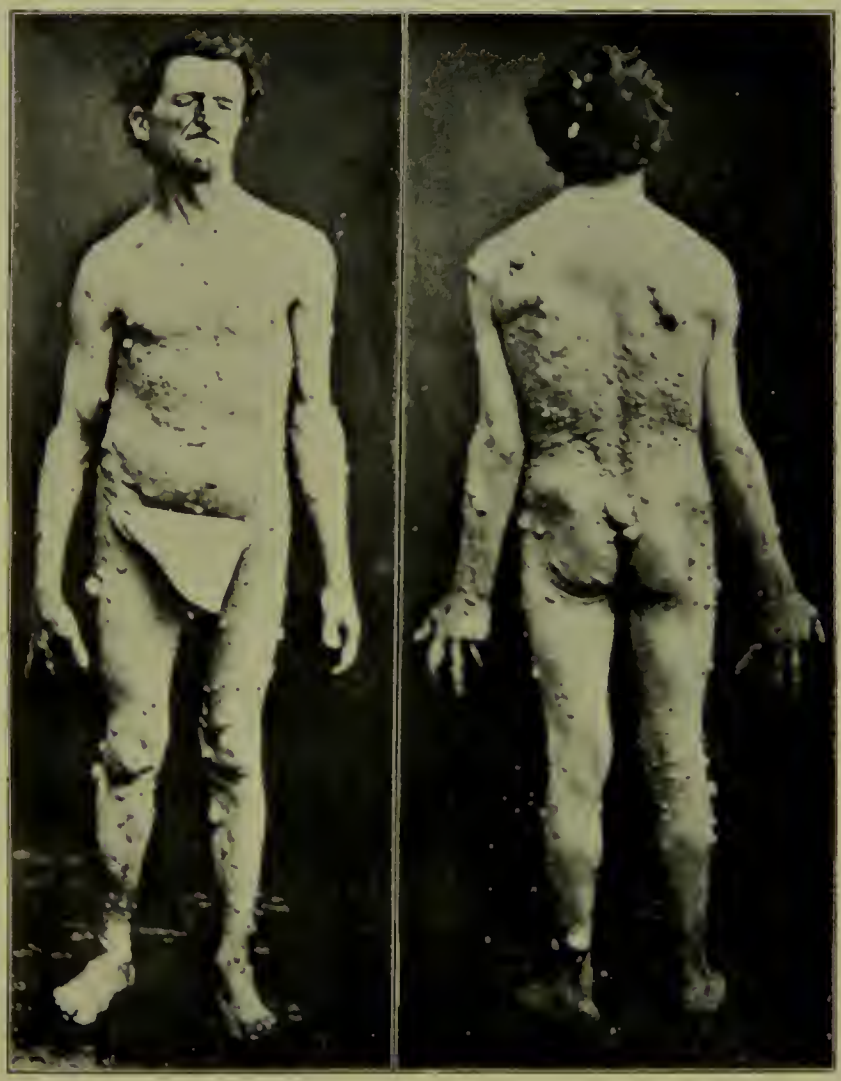
Our knowledge of the nerve origin of the multiple soft fibromata of the skin, known as molluscum fibrosum, dates from the publication of von Recklinghausen's well-known monograph in 1882. It is significant of the character of this work that the conclusions of its distinguished author have met with general acceptance, and have received the most ample corroboration down to the present day. The general characters of the multiple soft fibromata of the skin are fairly well known. We may quote the description given by von Recklinghausen of the two cases which came under his own observation, as classical types of the disease in question. The first case was a woman aged fifty-five who had died of pulmonary tuberculosis; she

was of dark complexion; almost the entire skin was studded with nodules or tumours. "Most of them project on the free surface and are pedunculated; some have a broad base. The majority are spherical. They are of every possible size, from a pin's head to an apple. They are covered by intact smooth skin. Some of them show one or more depressions on the free surface filled with sebaceous secretion. The tumours are most numerous over the breast, belly, and back, being so closely packed as to be in contact with, and flattened against each other; they are also numerous over the scalp, neck, and on the extremities, excepting the palmar surfaces of the hands and feet. The projecting tumours send prolongations of their substance into the subcutaneous tissue; others are quite subcutaneous and can be felt through the atrophied skin. Some are soft and flaccid, others are firm and solid; some give the impression of being lobulated or of being made up of a plexus of convoluted cords. They all consist of a soft white tissue, often partly transparent or opalescent. This tissue may be teased more or less completely into convoluted cords held together by a looser connective tissue."

"The skin of the body generally, especially the neck and trunk, is the seat of innumerable small brown pigment spots; there is a more diffuse brown pigmentation along the outer aspect of both thighs, around the external genitals, in the groins and over the shoulders. Over the projecting tumours the skin is paler and less pigmented than elsewhere." This patient was known to have had the cutaneous tumours since her earliest childhood. (There was fibromatosis also of the cutaneous nerves, of the nerve trunks of the extremities, of the sacral plexus, of the vagus, trigeminal, sympathetic, etc.)

Von Recklinghausen's second case (Plate XV.) was a labourer, aged forty-seven, who had had tumours of the skin ever since he could remember, and who stated that they had considerably increased in number after the age of fifteen. "The whole skin of the

PLATE XV.



Professor VON RECKLINGHAUSEN's case of multiple cutaneous neuro-fibromata.

body is studded with innumerable tumours resembling those described in the preceding case, except that on the extremities they are larger and more numerous ; some of them are pale like the surrounding skin, others present a darker or lighter rose tint, like that of a newly-born child. There is no excessive pigmentation as in the preceding case."

"On manipulating the tumours, one could recognise that while the smaller ones are quite uniform in consistence, others are lobulated, and others again are made up of convoluted cords, movable on each other, and arranged in the form of a plexus."

"There are also thickenings, enlargements, and palpable tumours in relation to the trigeminal vagus, and the nerve trunks of the limbs.

The microscopic examination of the cutaneous and subcutaneous tumours, showed that they were all of the nature of soft fibromata related to the terminal filaments of the cutaneous nerves, and that they resembled very closely the structure of the plexiform neuro-fibroma already described." The tumour tissue is either a succulent, spongy, feebly fibrillated tissue, rich in cells and well supplied with blood-vessels, or a tougher, more fibrous tissue, the fibres being arranged in bundles. There is neither any new formation nor any degeneration of the nerve fibres concerned. There is comparatively little dissociation of the nerve fibres, because the newly-formed connective tissue is for the most part situated between the bundle of nerve fibres and the investing perineurium ; the latter may form the capsule to the tumour, or it may lose its definition by fusion with the surrounding fibrous tissue. There are no elastic fibres in the tumours, except in the loose connective tissue uniting the different strands and masses which go to make up the tumour, and excepting also those which embrace the glands of the skin. The newly-formed connective tissue nearly always presents a plexiform arrangement resembling that observed in the plexiform neuro-

fibroma. The tubes of the sweat glands may be displaced and compressed; they may be dilated, or contain hyaline casts, and their ducts are often straightened out and lengthened. Many of the skin tumours are only the surface projections of tumours more deeply situated. "Von Recklinghausen believes that the skin fibroma usually originates in the deeper layers of the cutis, and especially in the stratum reticulare, and that it then grows in all directions, as well as towards the free surface. Had the fibroma arisen in the subcutaneous tissue, the sweat glands would have all been displaced towards the surface, whereas some of them are displaced downwards. The fibromata are always fixed to the overlying skin, differing from the lipomata, which originate in the subcutaneous fat and are easily shelled out. The sweat glands are merely accidental additions to or inclusions by the tumour; they may be entirely absent, *e.g.* on mucous membranes.

At the same time, von Recklinghausen believes that in addition to the sheaths of the cutaneous nerves, the sheaths of the blood-vessels, sweat glands, and ducts, and to a less extent, the sheaths of the hair follicles, are all implicated in the fibromatosis. The present concensus of opinion would appear to be, however, that the changes in the sheaths of the nerves are the primary lesion, and that the other structures and appendages of the skin are only implicated indirectly.

The impression gained by the author from the examination of the soft cutaneous tumours met with in one of his own cases, in which these were combined with multiple tumours on the trunks of the nerves, is, that what was observed clinically as a projecting tumour of the skin was not really a tumour at all, but a localised plexiform fibromatosis of the terminal filaments of the cutaneous nerves. A section right through the tumour showed the normal structures of the skin, *i.e.* fat lobules, sweat glands, blood-vessels, etc., permeated with nerve filaments, of which the majority had undergone fibro-

matosis, in consequence of which they were very greatly thickened, either uniformly or in the shape of tumour-like nodules. Unless the medullary sheaths of the nerve fibres had been stained dark blue one would have been unable to trace them, and one would have been apt to associate the fibromatosis and tumour-like nodules with the connective tissue sheaths of the arteries or of the sweat glands. The latter were merely displaced and compressed. The blood-vessels were abnormally developed, and in the deepest layers of the skin, or base of the tumour, they were dilated into sinuses, filled with blood like those in a cavernous angioma.

Von Recklinghausen contrasts the cutaneous neuro-fibroma with the lymphangio-fibroma met with in the form of soft warts on the face, neck, and back, in which the connective tissue cells are collected into clumps or strands corresponding to the lymphatic spaces and vessels of the skin and subcutaneous tissue in which the tumours have taken origin.

The distribution of the cutaneous neuro-fibromata is more often like that described in the typical cases of von Recklinghausen, viz., generalised over the whole body, excepting only the palms of the hands and soles of the feet. In exceptional cases they follow the distribution of one or more individual nerves. In one of my own cases there were only nine tumours altogether, and these were irregularly scattered over the trunk and limbs, in relation to different cutaneous nerves.

Simultaneous occurrence of skin tumours with other forms of neuro-fibromatosis.

In 26 of the recorded cases of molluscum fibrosum, the lesion was combined with tumours of the nerve trunks in 22, with pigmentation of the skin in 16, with plexiform neuro-fibroma in 6, and with elephantiasis neuromatosa in 2 cases. Molluscum fibrosum may also be associated with pigmented and other moles of the skin.

IV.—ELEPHANTIASIS NEUROMATOSA

In his famous lectures on morbid growths, Virchow differentiated from the other forms of congenital elephantiasis, one in which the nervous system participated; to this he gave the name elephantiasis neuromatosa. Its clinical features were well-known to the older writers, and were specially described by Valentine Mott of New York in 1854 under the name "Pachydermatocele." It has since been made the subject of investigation by Esmarch and Kulenkampf in their large work on elephantiasis, and by Jordan, Hürthle, Herczel, Westphalen, Czerny, Bruns, Pomorski, and others. The recognition of the nerve origin of certain forms of elephantiasis served to explain the occurrence of cases in which elephantiasis was met with in combination with other forms of neuro-fibromatosis, and the occurrence also of transition types.

Elephantiasis neuromatosa includes those forms of neuro-fibromatosis in which, in addition to the fibromatosis of the cutaneous nerves, there is also a pronounced and diffuse overgrowth of the skin and subcutaneous tissue in a particular region or segment of the body. It is not a strictly defined group, for transition forms are met with from molluscum fibrosum, and from the plexiform neuro-fibroma to elephantiasis; Bruns, and Esmarch and Kulenkampf, in fact, employ the last two terms indiscriminately. When the overgrowth of skin and subcutaneous connective tissue is met with in the head, neck or trunk,[1] it results in the formation of large tumour-like masses, often lobulated, and complexly folded, sometimes simulating the appearance of the folds of a curtain or of drapery. As they increase in size, they tend to hang down and to become pendulous or pedunculated. There is a gradual transition between molluscum fibrosum and elephantiasis. They are commonly the source of hideous and disgusting deformities. When growing from

[1] Their situation is commonly the same as the plexiform neuro-fibroma.

the scalp, they may hang down over the eye, and may lead to changes in the latter, resulting in loss of sight. The skin covering the growth may be smooth and natural, or it may be hard and uneven; it is frequently pigmented and thickened like a mole, and it may present an excess of hair. The tumour mass has a flabby feel, "like a relaxed and emaciated mamma" (Mott), and it is not uncommon to feel convoluted nerve cords running through the tumour, or to feel a bundle of such nerve cords in the neck of the tumour when it is pedunculated. In the case of the extremities (and especially the lower), the overgrowth may not present the appearances described, but rather the characters of a diffuse enlargement of the limb as a whole, closely resembling that met with in other forms of elephantiasis. According to Jordan, the overgrowth may not be confined to the skin and subcutaneous cellular tissue, but may involve all the tissues of the segment of the limb affected. The appearances of the lower extremity in cases of elephantiasis neuromatosa are well illustrated in Plate XVI. The whole limb is enormously enlarged and misshapen. In addition to the uniform enlargement, there may be separate pendulous masses or tumours separated from each other by deep folds or clefts. The consistence of the overgrowth may be soft and flabby, or it may be firm and resistant. The skin does not pit on pressure; it is usually thick, hard, coarse, and uneven, resembling morocco leather, or the hob-nailed surface of a cirrhotic liver.

The disease is of congenital origin, and usually begins in a brown spot or mole, or in a molluscum fibrosum which may, or may not, have been pigmented and furnished with hairs. The initial increase in size is imperceptible, and keeps pace with the growth of the individual; it may be more rapid after puberty; after many years, there are formed the enormous masses already described. They are not sensitive, and not abnormally vascular. There is no tendency to ulceration so long as the tumour mass is kept scrupulously clean

and protected from mechanical injury. The sensibility of the skin is usually somewhat blunted. The patient complains of the bulk, inconvenience, and unsightliness of the deformity. The transformation into sarcoma will be referred to later.

The anatomical characters of the elephantiasis neuromatosa have been studied in specimens which have been removed, and in limbs which have been amputated.

The skin and subcutaneous cellular tissue are enormously increased in thickness; the overgrown connective tissue presents a watery, glistening, greyish-white appearance, limited by the epidermis on the surface, and the fascia and muscles beneath. In parts it is soft and gelatinous and exudes an abundant watery fluid, in other parts it is whiter, drier, and fibrous. It replaces the normal cutaneous and subcutaneous fat more or less completely. Scattered throughout the tissue and embedded in it, are a variable number of fibrous nodules or tumours, isolated or in strings, and the latter may present the convoluted arrangement which is so characteristic of the plexiform neuro-fibroma. They may sometimes be shelled out from the looser connective tissue in which they are embedded. These fibrous nodules and strands represent a fibromatosis of the cutaneous nerves from which the more diffuse overgrowth of connective tissue is supposed to have originated. When sections of the affected tissues are examined microscopically, and stained after the method of Weigert, the following appearances may be observed. The special seat of the connective tissue overgrowth (as was also the case in the molluscum fibrosum) is in the pars reticularis of the corium, throughout which it extends indefinitely in all directions, displacing and replacing the normal fat, encroaching on the pars papillaris, flattening out the papillæ, and causing a partial disappearance of the regular and normal arrangement of the papillæ; on the deeper aspect of the corium the overgrowth extends into the subjacent cellular tissue. The sweat glands, although not

PLATE XVI.



Elephantiasis neuromatosa.

appreciably altered in structure, may be displaced ; when this takes place in a downward direction, the coils of the gland may be in immediate relation to the subcutaneous tissue, while their ducts are uncoiled, and are correspondingly lengthened. The hair follicles and sebaceous glands remain unchanged. The deeper layers of the epidermis frequently show an excess of the normal pigmentation. The Pacinian corpuscles may be greatly enlarged.

The fibrous nodules and strands embedded in the connective tissue overgrowth present very similar appearances to those observed in the plexiform neuro-fibroma, and in the molluscum fibrosum. The lesion is essentially the same. The special feature of the elephantiasis is the extension of the fibromatosis from the endoneurial connective tissue of the cutaneous nerves to the tissues surrounding them.

Degeneration of the nerve fibres involved in the fibromatosis has been recorded by more than one observer, but as in other forms of neuro-fibromatosis, the statement of its occurrence is to be accepted with reserve.

Changes have been described as occurring in the blood-vessels of limbs amputated on account of elephantiasis neuromatosa, by Jordan and Herczel, of the nature of endarteritis, and of thickening of the middle and outer coats ; Jordan goes further, and suggests that the fibromatosis originates in relation to the blood-vessels (and especially the capillaries), as well as in relation to the nerves.

Jordan has also observed degenerative changes in the muscles of the limbs similar to those met with in pseudo-hypertrophic paralysis.

Simultaneous occurrence of elephantiasis with other forms of neuro-fibromatosis.

While the most frequent combination observed has been that of elephantiasis with plexiform neuro-fibroma, numerous cases are on record of its co-existence with multiple tumours of the nerve

trunks, with multiple cutaneous fibromata, and with various forms of pigmentation of the skin. It is quite the exception for it to occur independently of one or other of these.

V.—PIGMENTATIONS OF THE SKIN ASSOCIATED WITH NEURO-FIBROMATOSIS

Reference has already been made to the occurrence of pigmentation of the skin in certain cases of neuro-fibromatosis, to the dark brown colour sometimes observed in the skin covering the plexiform neuro-fibroma, to the occasional origin of elephantiasis neuromatosa from a pigmented mole of the skin, and to the simultaneous occurrence of hairy and pigmented moles in certain cases of plexiform neuro-fibroma, and of elephantiasis neuromatosa. From my own analysis of seventy-six reported cases of generalised neuro-fibromatosis, there are no less than nineteen in which there was pigmentation of the skin, a proportion of twenty-five per cent. The pigmentation is merely an excess of that normally present in the skin, and is due to granules of pigment in the protoplasm of the cells of the rete Malpighii, and in the connective tissue corpuscles of the corium, and to a less extent in the intercellular tissue (Brigidi).

We may, following Feindel and Oppenheim, distinguish two varieties of this abnormal pigmentation; firstly, a punctiform variety, which is very like freckles (lentigo), only it is more often met with on the covered parts of the body, *i.e.* the trunk, and roots of the limbs, and usually spares the face and extremities. The pigment spots vary in depth of colour, and in number, and their distribution is, as a rule, quite irregular, being very rarely symmetrical, and very rarely following the distribution of any particular nerve or nerves.

The second variety is much rarer, it involves larger areas of the skin, which present a colour which has been likened to that of *café au lait*. The shape and distribution of these larger patches is quite

irregular; they are more often met with on the trunk, *e.g.* from the shoulders to the loins, or over one-half of the thorax and abdomen. The pigmentation may be present at birth, or it may appear later; it may remain stationary, or the spots or patches may increase in number and in size with increasing years.

Soldan, in a recent paper on the relations of pigmented moles to neuro-fibromatosis, records the results of his investigations in four cases of pigmented moles in which the latter were removed by operation, and were prepared and stained by the method of Weigert and Pal. He found that in every case the pigmentation and thickening of the skin was associated with a fibromatosis of the terminal filaments of the cutaneous nerves, and he formed the opinion that the pigmentation was in all probability a result of this fibromatosis, and that pigmented moles, in the majority of cases, are the first visible indications of a fibromatosis of the cutaneous nerves.

VI.—THE OCCURRENCE OF SARCOMA IN NEURO-FIBROMATOSIS

Secondary Malignant Neuroma (Garré).

The frequency with which the development of sarcoma has been observed in the subjects of multiple neuro-fibromata indicates that the association is more than a coincidence, and has led to the conclusion that the subjects of multiple tumours of the nerves are more liable to malignant disease than other people. Garré has the credit of demonstrating that the sarcoma which develops under these conditions, and to which he gave the name, "Secondary Malignant Neuroma," differs in several important particulars from that which develops in nerve trunks assumed to be normal, and which has already been described with the circumscribed and solitary tumours in Chapter III. It may be repeated in this place that the primary sarcoma of nerve trunks does not materially differ from sarcomata originating

in other tissues ; it exhibits the same rapid growth, the same tendency to infiltrate, and the same tendency to give rise to secondary growths in the internal organs. The "secondary malignant neuroma," on the other hand, is characterised by the rapid increase in size of a tumour which may have been in existence for years, and it may be from infancy, by the fact that it only infiltrates the surrounding tissues when it has recurred after removal, and that the recurrence is nearly always confined in the first instance to the nerve originally involved, or to other nerve trunks, and that it either does not give rise to metastases in the internal organs at all, or only at a very late stage in the progress of the disease. These views, promoted by Garré, have been corroborated by Scheven and others. The following case, observed by the author, is absolutely typical :—A man, aged twenty-eight, had suffered from multiple tumours of the peripheral nerves since the age of thirteen ; one of them, on the right median nerve at the elbow, had increased in size and become intensely painful during the twelve months before he applied for treatment. I removed this tumour and found it to be composed of the usual overgrowth of endoneurium, but at one point of the sections, there was a decided transition to a more cellular type of tissue suggesting a spindle-celled sarcoma ; the transition could be traced step by step from the branching cells of the endoneurial connective tissue. It recurred within four months, and again involved the median nerve ; it was also adherent to the surrounding tissues, and had fungated through the skin ; there were now evidences of paralysis in the distribution of the median nerve. The limb was amputated. The tumour was found to be an ordinary spindle-celled sarcoma. Ten months later, recurrence took place in the stump, and the limb was amputated at the shoulder joint. The growth was again a perfect type of spindle-celled sarcoma. Recurrence again took place in the vicinity of the scar. He lost flesh rapidly, and developed symptoms of a rapidly

growing tumour in the left lumbar plexus (painful contracture of the left lower extremity, pressure on the ureter, etc.) and died, a little more than two years after the first operation. On post-mortem examination, the viscera were found to be free from metastases. There was a spindle-celled sarcoma as big as a child's head involving the left lumbar plexus, the left psoas muscle, and the adjacent bodies of the lumbar vertebræ.

This case brings out very well the salient features of the "secondary malignant neuroma," and illustrates in a remarkable way that the sarcoma, grafted on the fibromatosis of a nerve trunk, while identical in structure with sarcomata of other origin, and while presenting all the features of local malignancy, instead of giving rise to metastases, is followed by the transformation into sarcoma of neuro-fibromatous tumours in other parts of the body. There are exceptional cases recorded, however, in which there were visceral metastases in "secondary malignant neuroma." Hume of Newcastle observed one in which, after removal of a sarcoma involving the sciatic nerve from a patient, the subject of neuro-fibromatosis, death took place from metastases in the lung, pleura, liver, and humerus. Westphalen records another case of generalised neuro-fibromatosis, in which a sarcoma developed in the popliteal space; the limb was amputated at the hip joint; metastases were found after death in the pleura and lung. A similar case is recorded by von Winiwarter.

As regards the relative malignancy of the primary sarcoma of nerve trunks, and the "secondary malignant neuroma," Garré's original view was that the latter was the less malignant of the two. While this may be true as regards its capacity for giving rise to secondary growths in the viscera, it does not hold so far as the danger to life is concerned. The list of cases of neuro-fibromatosis in which sarcoma has supervened, is one continuous record of deaths. As has been aptly pointed out by Scheven, the presumption is quite

the other way. Even after an early and successful operation for "secondary malignant neuroma," the patient is still the subject of neuro-fibromatosis, and is therefore liable to a fresh outbreak of sarcoma in some other part of his diseased nervous system. The primary sarcoma of nerve trunks being, to start with, a disease of purely local origin, is capable of complete eradication by surgical means. Goldmann apparently assumes that the local malignancy in "secondary malignant neuroma" may develop without any corresponding alteration in the structural characters of the original tumour. This is most unlikely, and is quite opposed to my own observations cited above. The malignant transformation in neuro-fibromatosis has frequently supervened on operative interference, or some other form of trauma; its occurrence is attended by the same degeneration and destruction of the nerve fibres involved, as in primary sarcoma of nerve trunks.

CHAPTER V

OTHER LESIONS OF THE NERVOUS SYSTEM MET WITH IN CASES OF NEURO-FIBROMATOSIS

It is a point of considerable interest to ascertain whether the central nervous system ever presents lesions which may be regarded as similar or allied to those which have been described in the peripheral nerves. The numerous records of post-mortem examinations of cases of neuro-fibromatosis might reasonably be expected to throw some light on this subject. I have collected the notes of forty-four cases in which a sectio was obtained; in only five of these is there any mention of a lesion of the central nervous system, and they may be briefly summarised as follows:—

1. *Neuro-fibromatosis with multiple tumours in the brain and cerebellum.*

Soyka records the case of a servant girl, aged twenty, who died of pulmonary tuberculosis. The neuro-fibromatosis specially affected the cauda equina, the intervertebral ganglia, the left brachial plexus, the sciatic, and the auditory and right optic nerves. There was a tumour as large as a walnut in the left lobe of the cerebellum compressing the pons; another the size of a hazel-nut in the right half of the cerebellum; a third, about 3 cm. in length in the upper part of the right optic thalamus; lastly, there were several pea-like tumours binding down the dura to the cerebral hemispheres. The nature of these tumours in the brain and cerebellum is not stated, but the probability is that they were tuberculous in character.

2. *Neuro-fibromatosis with cerebellar tumour.*

Soyka also records the case of a labourer, aged thirty-six, who died of broncho-pneumonia. The neuro-fibromatosis specially affected the spinal nerves in the cervical region and cauda equina, the intervertebral ganglia, the cervical and brachial plexuses, the sciatic, popliteal, and auditory nerves. In taking out the brain a bilateral tumour was found in the cerebellum, fused with the dura mater in the posterior fossa of the skull; the left half was as large as a walnut, the right as large as a hen's egg; the tumour was firm, fibrous, lobulated, with several cavities filled with a jelly-like substance.

3. *Neuro-fibromatosis with multiple tumours in the brain, cerebellum, etc.*

Generisch and Rump record the case of a man, aged thirty-nine, who first began to talk when seven years old, and then stammered very badly. He died of tetanus. There were multiple tumours on the nerve trunks, including the vagi and phrenics. On section of the brain circumscribed resistant nodules were found in the basal ganglia, most numerous on the right side, and having an average diameter of 1 cm. They were situated in the left optic thalamus, in the right lenticular nucleus and corpus striatum, in the cerebellar hemispheres, in the left corpus dentatum, and in both crura cerebelli. The ependyma of the ventricles was thickened.

4. *Neuro-fibromatosis with cerebellar tumour.*

Hesselbach and Heller report the case of a man, aged thirty-nine, who had suffered from the ordinary symptoms of cerebellar tumour. There were multiple tumours of the nerve trunks. The entire left half of the cerebellum was compressed by the greatly enlarged crus cerebelli; the right half was displaced. The pons Varolii was enlarged and tumour-like, and was not defined from the medulla or crura cerebri.

5. *Neuro-fibromatosis with diffuse glioma of spinal cord.*

Strube records the case of a sailor aged forty-five, who died of hæmoptysis, without having presented any symptoms referable to his nervous system. There were tumours of the nerve trunks, of the skin, and pigmentations of the skin. The anterior and posterior nerve roots were normal at their origin from the spinal cord. The ganglia on the posterior roots were as large as beans. There was a diffuse glioma of the cord, behind the central ependyma, and along the posterior median fissure. Strube discusses whether the simultaneous occurrence of neuro-fibromatosis of the nerves and glioma of the cord is a coincidence, or whether they are related to each other. He is inclined to regard them as independent developmental anomalies.

There is no information as to the histological structure of the intracranial tumours recorded in the first four cases. It is significant that the membranes of the brain and spinal cord, which are regarded as homologous with the sheaths of nerves, have never been observed to exhibit changes in any way resembling those characteristic of neuro-fibromatosis. The combination of tumours of the central nervous system with fibromatosis of the nerves, so far as our knowledge goes, would appear to be nothing more than a coincidence.

Recorded Cases of Neuro-Fibromatosis

No.	*Observer.*	*Age*	*Age at Onset.*	*Sex*	*Occupation*	DISTRIBUTION.	*Clinical Phenomena.*	*Mental and Other Peculiarities.*	*Complications.*	RESULT.
1	Abbe	9		f.		right cervical sympathetic and its communicating branches.	large tumour in neck of two months' growth, regarded as enlarged glands			tumour excised.
2	Barkow	30	28	m.	cattle-driver	vagi, rt. phrenic, nerves of extremities.	tumour in rt. calf grew to enormous size	weak intellect	repeated pleurisy	DIED. P.M. Phthisis.
3	Bruns	33	child-hood	m.		vagi, brachial plexus, sciatics, plexiform tumour left temple and eyelid.	plexiform tumour caused loss of sight of eye ; vagus tumour in neck caused hoarseness, loss of voice, difficulty of breathing ; v. marked heredity			DIED. P.M. Secondary hæmorrhage from oper. on vagus tumour.
4	Chavasse	30	26	f.		nerve roots within spinal canal (extra-dural), phrenics, nerve trunks generally and sympathetic, vagi.	tumour in neck thought to be glands ; excised ; nerve root torn from cord			DIED. P.M. Spinal meningitis after operation.
5	Czerny	25	birth	f.	field-worker	right lumbar and sacral plexus, sympathetic, elephantiasis of back and buttock, plexiform tumour of right thigh.	v. marked heredity ; operations on elephantiasis	never menstruated		DIED. P.M. Pyæmia after operation.
6	v. Büngner	36		f.		vagi and nerves generally, spinal nerve roots within dura compressing cord.	successive development of tumours and successive operations ; paraplegia, contracture, par. of bladder		broncho-pneumonia	DIED. P.M.
7	Feindel	58	50 ?	m.	labourer	skin pigmentation since childhood, multiple tumours of skin.	sarcoma of rt. popliteal nerve ; amputation of thigh	sensitive and "modest"	sarcoma	?
8	Finotti	44	child-hood	f.		skin tumours since childhood, tumours of nerve trunks.	spindle-celled sarcoma of left sciatic excised		sarcoma	DIED. ' Sarcoma.
9	Gerhardt	30	early youth	m.	labourer	cranial nerves except optic and auditory, all spinal and peripheral nerves, sympathetic in lungs, liver, pancreas, etc.	left-sided hemiparesis, then paraplegia, from compression of cord	stupid, empty expression	typhoid	DIED. P.M. Typhoid perforation.

10	Generisch and Rump	39		m.		vagi, phrenics, nerves generally.	Brothers Pfeiffer.	headaches from childhood	only spoke at age of seven, then stammered; mentally deficient; small penis	multiple tumours in basal ganglia	Died. P.M. Tetanus.
11	Generisch	22	8	m.	shoemaker	3, 4, 5 cranial nerves and vagus, nerves generally.		diarrhœa, difficult micturition, bedsores	epispadias, voice like a child	pneumothorax bronchopneumonia	Died. P.M. ? Sarcoma.
12	Goldmann	54	early youth	f.	housewife	subcutaneous tumours and pigment spots since early youth; tumour median nerve, plexiform tumour intercostal nerve.		sarcomatous transformation of intercostal tumour; excised, recurred, again excised		sarcoma	Died. P.M. Sarcoma.
13	Hensinger	23		m.	tailor	5th, hypoglossal, and vagus, nerves generally, sympathetic extensively involved.		diagnosed as tuberculous			Died. P.M. Phthisis.
14	Hasler and Schönlein	20		f.		rt. vagus, nerve roots in spinal canal in cervical region. sympathetic.		pains in arms, anæsthesia, paralysis, contracture, could not stand or sit or hold head up, emaciation		difficult breathing	Died. P.M. Suffocation.
15	Hesselbach Heller	39	skin tum'rs since birth	m.	plasterer	multiple skin tumours, nerves generally, sympathetic.		symptoms of cerebral tumour		tumour crus cerebri and pons	Died. P.M.
16	Herczel	9	7	m.		plexiform left brachial plexus, pigmentation and elephantiasis left arm, nerves generally.		tumours and elephantiasis subjected to operation			Disease progressing twenty months after operation.
17	Herczel	10	2	f.		plexiform behind ear and in upper arm, pigmented elephantiasis of arm, pigmentation over trunk nerves generally.		excision of plexiform tumour	backward mentally		?
18	Herczel	36	birth	f.		pigmentation on trunk and limbs, multiple cutaneous tumours.		some cutaneous tumours excised			?
19	Hodsdon	17	9	f.	dressmaker	plexiform rt. median nerve upper arm, pigmentation over trunk and limbs, nerves of arm and hand.		occasional pains in arm; plexiform tumour partially excised			Still under observation.

Recorded Cases of Neuro-Fibromatosis—*continued*

No.	*Observer.*	*Age*	*Age at Onset.*	*Sex.*	*Occupation*	Distribution.	*Clinical Phenomena.*	*Mental and Other Peculiarities.*	*Complications.*	Result.
20	Hitchcock	46	25	m.		multiple subcutaneous tumours; tumour on ulnar nerve above int. condyle.	indolent course of ulnar tumour for twenty years, then rapid growth; excised, recurrence, amput. at shoulder		sarcoma	Died seven months after operation
21	Hartmann	48	34	f.		nerve trunks generally.	rapid growth of tumour in axilla after fourteen years' indolence		sarcoma	?
22	Hume	37	child-hood	m.		tumours of skin and of nerve trunks.	rapid growth of tumour of left sciatic, excised		sarcoma	Died. P.M. Sarcoma in pleura, lung, liver, humerus.
23	Haber-mann	28		f.		skin tumours, moles, pigmentation elephantiasis, nerve trunks.	rapidly growing tumour of sciatic removed; do. of ulnar nerve		sarcoma	?
24	Hankins	39	27	f.		pigmentation since childhood; warts, moles and multiple tumours of skin, nerve trunks.	sarcoma in neck excised, tumour of musculo-spiral removed, recurrence in neck		sarcoma	Expected to die.
25	Heller	45		m.	school-teacher	spinal nerves from 2nd lumbar, nerve trunks, sympathetic.	extensive leg ulcer	cryptorchismus		Died. P.M. Of pneumonia two days after amput. of leg.
26	Hürthle and Nauwerck	22		m.		multiple skin tumours, large molluscum fibrosum rt. thigh, vagus, cauda equina, nerves generally.		weak intellect		Died. P.M. Cachexia.
27	do.	35		m.		molluscum fibrosum on trunks and arms, elephantiasis both lower limbs.	stunted growth, emaciated, kypho-scoliosis	very deficient mentally		Died. Exhaustion.
28	Jordan	23	early child-hood	f.		subcutaneous tumours, elephantiasis left leg.	amputation of thigh	stupid face, low intelligence		?

29	Jordan	17		f.		pigmentation face and body, elephantiasis right lower limb, subcutaneous pea-like tumours.	amputation of thigh	intellect much below average		DIED. General weakness
30	Knoblauch and Bischoff	38		m.		tumours on cranial nerves except 1st, 2nd, 5th, nerves generally, sympathetic.		idiot from infancy	gangrene of lung and pleurisy	DIED. P.M.
31	Kriege	62		f.		pigmentation and tumours of skin, nerve trunks of thigh, hypoglossal.			dropsy and broncho-pneumonia	DIED. P.M.
32	Kupferberg	60		m.	butcher	cauda equina, nerves lower limbs.				DIED. P.M.
33	Launois and Variot	21	9	m.	shoemaker	5th cranial and nerves generally; sub-cut. tumour rt. thigh since age of nine.	tumour of thigh excised; cramps, contracture, emaciation, vomiting; recovery under potassium bromide			?
34	Leboneq	26		m.		3rd, 5th, vagi, phrenics, intercostals, cauda equina, nerves of limbs.	paralysis, opisthotonus—diarrhœa			DIED.
35	Menke	23		m.		plexiform tumours, nerve trunks generally.	tumour growing from lumbar nerves excised	inclined to be an idiot		?
36	de Morgan	15	birth	f.		elephantiasis of hand from birth; plexiform and radial nerve in forearm, nerve trunks of arm.	sarcoma of radial tumour at age of twenty-two; amputation above condyles; recovery		sarcoma	In good health.
37	Morel Lavallée					vagi, nerves generally.			cholera	DEATH. P.M.
38	Launois and Variot	57	42	m.		nerve trunks of limbs—axillæ.	weakness of limbs, emaciation			?
39	Maric	54		m.		tumours and pigmentation of skin, subcutaneous nodules, nerves of forearm.	dull, resigned, apathetic, impaired memory, extensive anæsthesia		chronic arthritis	?
40	Nélaton Houel	26		m.	shoemaker	3rd, 5th, facial, vagus, opthalmic and Gasserian ganglia, cauda equina, sympathetic, nerves generally.	severe pain, contracture of forearms and legs; tumour in rt. groin excised; increase in number of tumours, emaciation, diarrhœa, bedsores		difficult respiration, paraplegia	DIED. P.M.

Recorded Cases of Neuro-Fibromatosis—*continued*

No.	*Observer.*	*Age*	*Age at Onset.*	*Sex.*	*Occupation*	Distribution.	*Clinical Phenomena.*	*Mental and Other Peculiarities.*	*Complications.*	Result.
41	Péan	25	4	m.		nerve trunks generally.	severe pains left arm ; tumour median nerve excised	supernumerary right testicle		?
42	Pomorski	28		m.	fisherman	pigmentation, warts and tumours of skin, nerve trunks generally, ploxiform tumour of intercostal nerves.	pains in rt. chest, dyspnœa ; hæmorrhagic effusion into pleura tapped ; diagnosed sarcoma, ascites		intercostal tumour pressed on infer. vena cava	Died. P.M.
43	Payne	37	childhood	f.		tumours and pigmentation of skin, subcutaneous nodules, tumours in brachial plexus.	skin tumours observed for six years, some wasted and disappeared, fresh ones formed		diarrhœa, vomiting, syncope	Died. P.M.
44	Prudden and Satterthwaite	25		f.	lady's maid	optic, trigeminal, vagus, spinal accessory, hypoglossal, nerves generally, sympathetic.	pains in sciatic nerves ; leucocytosis		diarrhœa, vomiting	Died. P.M.
45	von Recklinghausen	47	childhood	m.	labourer	multiple tumours of skin, of supraorbital, nerves generally.	increase of skin tumours after age of fifteen	stammers		?
46	do.	55	3	f.		multiple tumours of skin, and pigmentation, trigeminal and vagus, sacral plexus, cutaneous nerves, sympathetic.	never any nerve symptoms		pulmonary hæmorrhage	Died. P.M. Tuberculosis.
47	Rolleston	32	birth	m.		pigmentation, large molluscum fibrosum, vagi, nerves generally.	sarcoma of left brachial plexus, pressing on bronchus and causing paralysis of ulnar nerve and sympathetic, emaciation		sarcoma, dyspnœa	Died. P.M.
48	Schlange	15		m.		pigmentation and tumours of skin, nerve trunks generally.	emaciation, cachexia	stupid expression, dull intellect, asymmetrical skull	pleural effusion	Likely to die.
49	R. W. Smith	32	31	m.	farmer	vagi, phrenics, nerves generally. 2000 tumours.	onset preceded by mental distress, sleepless, restless, emaciating		vomiting, diarrhœa	Died. P.M.

50	R. W. Smith	35	20	m.	cattle-driver	left hypoglossal, phrenics, nerves generally.	sciatic tumour as big as patient's head, cachexia		? sarcoma	DIED. P.M.
51	do.	45	29	m.	gentleman	nerves of limbs.	fresh tumours developed while under observation			Good health.
52	Sibley	45	38	m.	coach-painter	vast number of tumours within spinal canal, one as large as nut; constricted cord opposite 2nd and 3rd cervical vertebræ.	four years motor and sensory paraplegia, partial of upper limbs, contracture, paralysis bladder and rectum, bedsores		paraplegia, bed-sores, etc.	DIED. P.M.
53	Soyka	20		f.		both auditory nerves, optic on rt. side, cauda equina, nerves generally.	symptoms of brain tumours, ? tuberculous	stuttered since childhood, had to be sent to asylum	multiple tumours of brain	DIED. P.M. Tuberculosis.
54	do.	36		m.	labourer	both auditory nerves, intradural tumours on cervical nerves and cauda equina, nerves generally.	symptoms of brain tumour	deficient intelligence	tumour of cerebellum	DIED. P.M.
55	T. Smith	65	20	f.		nerves of forearm.				DIED. P.M. Of other causes.
56	Schiffner	34		m.	brothers	vagi, spinal accessory, sympathetic, nerves generally.	unable to walk till seventh year, then convulsions	cretin from birth	apoplexy	DIED. P.M.
57	do.	33		m.	brothers	trigeminal, facial, glosso-pharyngeal, vagi, spinal accessory, cervical and brachial plexus, nerves generally.	paraplegia several years	cretin from birth	paraplegia	DIED. P.M.
58	Strube	45	20	m.	sailor	pigmentation and tumours of skin since twenty, 5th, vagi, sympathetics, intervertebral ganglia.	no nerve symptoms, haemoptysis		diffuse glioma cervical cord, phthisis	DIED. P.M.
59	Scheven	24	20	m.	watch-maker	pigmentation of skin, vagi, sympathetic, nerves generally.	sarcomatous transformation of left median tumour at elbow, excised, recurred, excised, recurred, amputation, death		sarcoma, pneumonia	DIED. P.M.
60	Serres	23		m.	glazier	vagi, sympathetic, nerves generally, 500 tumours.	no nerve symptoms		typhoid ?	DIED. P.M.
61	do.			m.	weaver	vagi, sympathetic, nerves generally.	no nerve symptoms; sciatic as big as adult humerus		typhoid ?	DIED. P.M.

Recorded Cases of Neuro-Fibromatosis—*continued*

No.	*Observer.*	*Age*	*Age at Onset.*	*Sex.*	*Occupation*	Distribution.	*Clinical Phenomena.*	*Mental and Other Peculiarities.*	*Complications.*	Result.
62	Serres	26		m.	convict	all cranial nerves, nerves generally.	sad and gloomy after sentence, apathetic, emaciation, diarrhœa, no nerve symptoms		typhoid ?	Died. P.M.
63	do.	26		m.	carpenter	nerves generally.	blind right eye and ptosis, pains in limbs, emaciation, choking attacks			Likely to die.
64	Salomon	21		m.	joiner	pigmentation of skin, supra-orbital and facial, nerves generally.	only certain tumours painful ; an increase in number observed	weak intellect ; in imbecile institution since age of nine		?
65	Tietze	27	7	f.	servant	tumours of skin, plexiform tumour left side of head above ear, tumours in rt. side of neck and trunk.	plexiform tumour excised			In good health.
66	Temoin	32	15	m.		vagi, sympathetic, nerves generally.	rapid growth of tumour of right radial, excised ; pyæmia		? sarcoma	Died. P.M. Pyæmia after operation.
67	Alexis Thomson	56	23	m.	mason	nerve trunks lower extremity.	tumours are sensitive and cause pains ; excised, recovery			In good health.
68	do.	16	14	f.	school-girl	plexiform left small sciatic, multiple subcutaneous nodules trunk and limbs.	no symptoms ; partially excised ; continued to grow			Quite well 3 years later.
69	do.	25	18	m.	bookseller	tumours of skin, nerve trunks generally.	pains, loss of flesh and strength, excision of tumours, more active growth, malignant transformation		? sarcoma	Died.
70	do.	28	13	m.	labourer	tumours of skin, nerve trunks generally.	severe pain and rapid growth of median nerve tumour ; excised, recurr., amput., recurr., amput., recurr., death		sarcoma	Died. P.M.

71	Alexis Thomson	41	37	m.	wool spinner	within spinal canal and upon nerves generally.	irregular paralysis of all four extremities	influenza	DIED.
72	Westphalen	45	35	f.		tumours and pigmentation of skin, facial, lingual, vagi, hypoglossal, nerves generally.	sarcomatous transformation of tumour in brachial plexus	sarcoma, septic pneumonia. pericarditis	DIED. P.M.
73	do.	35	childhood	f.		tumours and pigmentation of skin, left optic, left vagus, left phrenic, nerve trunks generally.	sarcomatous transformation of popliteal tumour; amputation at hip, death	sarcoma pleura, lung, etc.	DIED. P.M.
74	von Winiwarter	36	8	m.		plexiform tumour of shoulder and arm, nerve trunks of arm.	sarcomatous transformation of plexiform tumour; excision, gangrene, amputation, death of septic infection	sarcoma lung, etc.	DIED. P.M.
75	Wilks	25		f.	prostitute	vagi, nerves generally.	phthisis	phthisis	DIED. P.M.
76	Wegner	adult	childhood	m.		tumours of skin, vagi, sympathetic, nerves generally.		typhoid	DIED. P.M. Perforation of intestine
77	Koeppelin	23	childhood	f.		pigmentations of skin, plexiform tumour of cheek, tumours of thigh, neck, and trunk.	tumour of cheek removed because of deformity		Still under observation.

The general pathology of neuro-fibromatosis may be discussed under the following heads :—

1. The period of onset.
2. The influence of heredity.
3. The simultaneous occurrence of other defects of developmental origin.
4. The influence of sex.
5. The influence of external factors on the development of neuro-fibromatosis.
6. Theories as to the origin of neuro-fibromatosis.
7. The occurrence of neuro-fibromatosis in the lower animals.

1. *The period of onset of neuro-fibromatosis.*

Inasmuch as fibromatosis of the nerve trunks may not attract notice until tumour-like enlargements have formed which are capable of being recognised on clinical examination, it is impossible to determine the period of its onset with any approach to accuracy. We have more definite information regarding the external and visible manifestations of neuro-fibromatosis in the shape of pigmentations and tumours of the skin, and of elephantiasis. The skin tumours and pigment spots have been frequently observed at birth, or are stated to have been present from early childhood. In some cases the pigmentation has been present at birth, and the tumours have appeared later. Either or both of these may thereafter remain stationary, or they may increase in size and number; there may be a decided increase at puberty; fresh tumours or spots may appear at any subsequent period of life, or certain of the older ones may disappear, so that they may actually diminish in number and in size with advancing years.

Elephantiasis may be present at birth, or may develop in child-

hood, and may be in relation to a mole which was present at birth; I am not aware of any case commencing after puberty.

The plexiform neuro-fibroma resembles the elephantiasis with which it is commonly associated, inasmuch as it may be present at birth, or develops in early infancy.

With regard to the generalised fibromatosis of the nerve trunks, there is a want of accurate information as to its initial development or onset. Patients with tumour-like enlargements of the nerve trunks may be able to tell that the latter have been present for many years, or as long as they can remember. They have been stated to have been present at the age of four (Péan), nine (Hodsdon, Abbé, Launois, and Variot), thirteen (Alexis Thomson), fifteen (Temoin), etc. (The ages in the remaining cases are shown in the Table on page 92.)

It is only reasonable to assume that the disease had existed long before it was capable of being recognised, and that the probable period of origin of the disease is either in intra-uterine life, or in early childhood or adolescence. I am not aware if the bodies of infants have been examined systematically for evidence of neuro-fibromatosis; it may be taken for granted that any pronounced thickening of the nerves, and more especially of the sympathetic nerves within the thorax or abdomen, is never present at birth, or it could hardly have been overlooked in the numerous post-mortem examinations of still-born and other infants. The microscopical examination of the nerves of infants by modern methods might, however, yield important information.

2. *The influence of heredity.*

This has attracted the interest of most writers on neuro-fibromatosis. The available facts are as follows :—

Observer.	*Nature of Case Recorded.*	*Relatives Affected.*	
Generisch and Rump	two brothers Pfeiffer, aged 22 and 39; multiple tumours of nerve trunks	mother,	multiple tumours in axilla.
Hesselbach and Heller	male, aged 39; multiple tumours of skin and nerve trunks	father,	multiple skin tumours.
Schiffner	two brothers Säulich, aged 33 and 34; both had multiple tumours nerve trunks		
Herczel	girl of 10; plexiform and other tumours, pigmented elephantiasis	mother, grandfather,	multiple tumours of skin.
Czerny	female, 25; elephantiasis of buttock, plexiform and other tumours of nerves	maternal great grandfather,	skin tumours.
		maternal grandfather,	large solitary skin tumour.
		maternal grand-uncle,	large solitary skin tumour.
		maternal uncle,	large multiple skin tumours.
		mother,	large solitary skin tumour.
Hitchcock	male, 46; tumours of nerve trunks	mother and sister,	tumours of nerve trunks.
Rolleston	male, 32; molluscum fibrosum, pigmentation of skin, tumours of nerve trunks	patient's child,	pigmentation of skin.
Salomon	male, 21; pigmentation of skin, tumours of nerve trunks	sister,	pigmentation of skin.
Bruns	two brothers, plexiform tumour and elephantiasis		
Bruns	male, 18; plexiform tumour, pigmentation of skin, subcutaneous tumours	paternal grandfather, father, and three brothers,	subcutaneous tumours similar to those of patient.

The above facts demonstrate that neuro-fibromatosis is sometimes inherited, and is sometimes met with as a family disease; they lend support to the view that the chief etiological factor in the disease is one which dates from intra-uterine life.

3. *The simultaneous occurrence of other defects of developmental origin.*

While it is true that the majority of the recorded patients with

generalised neuro-fibromatosis were healthy and well developed in other respects, there was still a considerable number in which there existed some mental or bodily defect of developmental origin as, for example, the well-known cretin brothers, recorded by Schiffner, and Knoblauch's patient, who was an idiot from birth, while in fourteen carefully reported cases, the patient is described as being of an inferior type, stupid, and weak mentally. Stammering was a prominent feature in four cases. Bobrow observed a boy aged ten, with left-sided macroglossia along with a plexiform tumour of the left side of the head and occiput. Strube's case, in which there was a diffuse glioma of the spinal cord, along with extensive neuro-fibromatosis, has already been referred to.

Sexual defects of developmental origin have also been observed. Generisch reports the case of a man, aged twenty-two, with multiple tumours of the nerve trunks, who had a voice like a child, and a well-marked epispadias, and another in which the penis was small and the sexual instinct undeveloped; Heller reported one with undescended testicles, and Péan one with a supernumerary testicle; Czerny's well-known case of elephantiasis was a female, aged twenty-five, who had never menstruated.

4. *The influence of sex.*

There is nothing to indicate that the question of sex has any bearing on the etiology of neuro-fibromatosis. In the eighty-four cases in which the sex is mentioned, fifty-three were males and thirty-one females.

5. *The influence of external factors in the development of neuro-fibromatosis.*

There is no evidence to show that neuro-fibromatosis is ever the result of any external influence. There is no suggestion that it may be due to any intoxication (alcohol, arsenic), or to any infective

process (syphilis, leprosy, diphtheria). It is possible, however, as in other inherited and family diseases, that external factors may influence the period of its development, the localisation of the morbid process, and the rapidity of its progress. The visible outbreak of generalised neuro-fibromatosis has been ascribed to exposure to cold and wet, to the depressing influence of intercurrent disease, to mental distress, and to traumatism. It seems more probable that these may play the part of accelerating or aggravating influences, than that they are capable of actually exciting the development of the disease. The importance of injury, as an exciting factor, was drawn attention to by R. W. Smith, who spoke of "traumatic neuroma"; it is certain, however, that while injury, or an embedded foreign body, may be quite capable of causing a local enlargement of the nerve affected, it never gives rise to the generalised disease. Such antecedents as eczema or boils, on which stress may be laid by patients, are to be regarded in a similar light. External factors may, however, have a considerable influence in the localisation of the disease. The plexiform tumour is alleged to have developed in the site of a previous injury. In relation to the cutaneous neuro-fibromata, it was pointed out by von Recklinghausen that they were most numerous where there was most friction and pressure, (around the waist in women; over the neck, shoulders, back, sacrum and occiput, in both sexes); while their absence from the palms of the hands and soles of the feet was ascribed to the protection afforded to the nerves by the thick pad of fat in these situations. The influence of operative interference when the disease has developed, will be considered along with the clinical features.

6. *Theories as to the origin of neuro-fibromatosis.*

It must be confessed at the outset that the actual origin of neuro-fibromatosis is quite unknown. It has been presented in the pre-

ceding chapters as a disease which, while confined to the peripheral nervous system, may be distributed throughout its whole extent, viz., the cerebro-spinal nerves, the sympathetic nerves, and the nerve terminations in the skin and these may be regarded as constituting one organ, both from the developmental, structural, and functional points of view. From the facts which have been already stated, viz., that it may be inherited, that it may run in families, that it may be present at birth or appear in early life, or at any rate before maturity, and that it may be associated with other developmental errors, Neuro-fibromatosis would appear to be a developmental disease of this organ, dating from intra-uterine life. The central nervous system has never been observed to participate in the fibromatosis. It is remarkable that the membranes of the brain and spinal cord, which are generally regarded as homologous with the connective tissue sheaths of the nerves, show a similar exemption from any disease resembling neuro-fibromatosis. It may be that a more accurate knowledge of the development of the peripheral nervous system may shed some light on its origin. We cannot agree with Feindel, who endeavours to sustain the hypothesis that generalised neuro-fibromatosis is the result of a primitive malformation of the ectoderm, for the most important derivative of the ectoderm, viz., the central nervous system, remains unaffected. So far as our present knowledge goes, I think we are warranted in adopting the view expressed by Bruns, Goldman, and others, that the condition is a form of giantism or elephantiasis of the connective tissue elements of the peripheral nervous system.

7. *The occurrence of neuro-fibromatosis in the lower animals.*

Multiple neuromata have been observed by veterinary surgeons in the lower animals, especially in the horse and cow. The disease presents the same features as in the human subject. We

may refer to the frequently quoted case observed by Colin,[1] on examining the carcase of an apparently healthy cow, he found innumerable tumours of the nerves, especially the sympathetic and visceral plexuses, but also in the nerves of the tongue, neck, and forefeet. The largest of them weighed five lbs., and was situated in the solar plexus, surrounding the anterior mesenteric artery.

[1] Colin. "Récueil de Médecine Vétérinaire." Série IV., T. VIII., p. 947.

CHAPTER VI

CLINICAL FEATURES OF NEURO-FIBROMATOSIS

The period of onset, the influence of heredity, of sex, and of external factors on the development of generalised neuro-fibromatosis, have been discussed in the preceding chapters. The clinical features may be considered under the following heads :—

1. Symptoms and signs referable to the enlargement of the nerves.
2. Clinical course and terminations of the disease.
3. Diagnosis, prognosis, and treatment.
4. Special features of the plexiform and elephantiasis varieties of the disease.

1. *Symptoms and signs referable to the enlargement of the nerves.*

The fact that the disease has been discovered more than once on post-mortem examination when its existence was entirely unsuspected during life, indicates that it may occur in a latent form and that even an extensive neuro-fibromatosis may be unattended by any symptoms. This specially refers to what may be called *the first or initial stage* in the development of the malady, which may be said to exist only in a pathological sense. The existence of neuro-fibromatosis is not revealed until the local exaggeration of the process results in the formation of one or more "tumours"; this may be described as *the second stage* of the disease.

The presence of tumours or of palpable enlargements of the nerves.

The recognition of "tumours" of the nerve trunks is only possible when these are accessible to clinical examination, *e.g.* in the extremities, neck, walls of the thorax and abdomen. Their physical characters have been already described (Chapter IV.). In shape they are elliptical or fusiform, with the long diameter in the axis of the nerve; occasionally they are spherical or even somewhat flattened when confined by a strong fascia or other resisting structure; they are freely movable transversely, but not longitudinally. They may be soft, firm, or even fibrous in consistence. Their distribution may be to a certain extent symmetrical in correspondence with the normal bilateral symmetry of the nerves themselves. They vary in number from one or two to many hundreds, and in size from the most minute nodule, to growths of considerable proportions. The small pin-head or pea-like nodules are frequently met with along the cutaneous nerves of the extremities, and in the subcutaneous tissue of the thoracic and abdominal walls (Plate XVII.). The larger tumours are more often met with in the large nerve plexuses; when originating in the brachial plexus they may appear as a large mass above the clavicle, or in the axilla; in the lumbar and sacral plexuses as an abdominal or pelvic tumour. Tumours of medium and occasionally of large size, are met with in the nerves of the extremities, viz., the median and ulnar nerves especially, in the upper arm, the sciatic in the buttock or back of the thigh, the popliteals in the ham, and the anterior crural in the upper part of Scarpa's triangle. (A more complete account of the distribution of the tumours has been given in Chapter IV.)

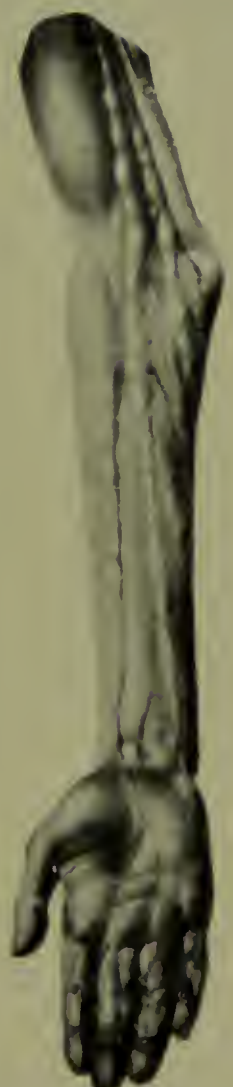
In addition to what may be called tumours, one may identify other diffuse and extensive enlargements of the more superficial nerves, especially in emaciated subjects (Plate XVIII.).

PLATE XVII.



Multiple subcutaneous neuro-fibromata.
(From one of R. W. Smith's cases of generalised neuro-fibromatosis.)

PLATE XVIII.



The right upper extremity from one of R. W. Smith's cases of generalised neuro-fibromatosis. The thickened and beaded nerves are visible through the skin.

Symptoms resulting from the fibromatosis of the peripheral nerves.

In striking contrast to the solitary tumours of nerves, which are remarkably sensitive, the multiple "tumours" are usually quite insensitive, so that their existence may be unknown to the patient, or they may have obtruded so little on his attention, that he is unable to say whether they appeared together, or in succession, and he may be unable to give any information as to the date of their first appearance. Very commonly there is one particular tumour of which he complains, and he may be ignorant of the existence of the others. The sensitive tumour is usually one which is exposed to pressure or injury, *e.g.* involving the nerves of the upper arm or at the bend of the elbow, the sciatic in the buttock, the external popliteal over the neck of the fibula. There is less likely to be any complaint of tumours which are better covered by soft parts, *e.g.* the sciatic in the mid thigh, the anterior crural in Scarpa's triangle, the vagus in the neck, and those in the interior of the thorax and abdomen. Sensitiveness is not however altogether a question of exposure to pressure, for the minute subcutaneous tumours which may be present in hundreds along the intercostal and other cutaneous nerves are almost without exception quite insensitive, resembling in this respect the skin tumours proper, but in marked contrast to the "solitary painful subcutaneous tubercle." Sometimes the sensitiveness of a particular tumour appears to depend on its having grown more rapidly; it is then sometimes a little fixed or adherent to the surrounding tissues. Apart from the possibility of more rapid growth on exposure to injury, no satisfactory explanation has been given why, in a case of multiple tumours, the majority may be freely handled, and one, or it may be two or more, may be so sensitive that the slightest pressure causes agony which may last for hours. In one particular case, which was under my own observation for over two

years, the sensitiveness of individual tumours varied to a remarkable degree from time to time ; certain of them which were quite insensitive when the patient first came under observation, became exquisitely tender when the disease was further advanced. The only explanation I can suggest is, that the sensitiveness is associated with changes in the nerve fibres involved by the tumours ; certain it is, that when a tumour undergoes sarcomatous transformation, the sensitiveness and pain are very pronounced, and are associated with destructive changes in the nerve fibres. The nerve trunks themselves, apart from the presence of tumours, may be sensitive. Other sensory disturbances are exceptional, *e.g.* blunting of sensibility to touch, pain, and temperature. Actual anæsthesia is very rare.

Disturbances of the motor functions are also very exceptional ; cramps of the muscles supplied by the nerve involved by the tumour, reflex spasm in adjacent or even distant muscles, involuntary jerkings of a limb, may be observed on handling the tumour ; they are very rarely spontaneous. Impairment of muscular power is not uncommon, but it is more often the result of the sensitiveness of tumours than of actual paresis or paralysis ; the occurrence of paralysis may be regarded as evidence of the pressure of tumours on the spinal cord, or nerve roots within the spinal canal, or of the development of sarcoma. Tumours on the nerve fibres in the substance of a muscle may be sensitive, and on squeezing them the muscle may pass into a condition of spasm.

Symptoms from pressure on the spinal cord and nerve roots.

Pressure on the cord is produced by the tumour-like enlargements of the nerve roots within the spinal canal. These have already been described as most frequent in the cervical region, and in the cauda equina. A solitary case is recorded by Gerhardt in which a tumour of the spinal accessory nerve, where it passes through the foramen magnum, pressed on the medulla oblongata.

The symptoms resemble those met with in other forms of compression of the cord (*e.g.* Pott's disease); they are very gradual in onset, and they vary very much at different periods; they may improve in a remarkable way, and then relapse; this is probably associated with variations in the consistence, tension, and size of the tumours, depending on alterations in the amount of blood and lymph in their substance. The cord symptoms include motor paresis or paralysis of the legs, less frequently of the arms as well, very rarely of one side of the body or of the muscles of the trunk or neck; in the case of the limbs the paralysis may go on to flexor spasm and contracture, so that the patient may become crippled and bed-ridden. Paralysis of the bladder and rectum, a tendency to bed-sores, and alterations in the reflexes have been observed in several cases.

Sensory symptoms are decidedly less frequent, *e.g.* pains in the limbs, formication, anæsthesia, painful cramps, sensory paraplegia.

The cord symptoms are well illustrated in a case observed by the author over a period of three and a half years. The patient, a man aged forty-one, first complained of a dull heavy pain in the back, the sensation of pins and needles with occasional twitching in the right foot, which then began to drag in walking. On stooping he had difficulty in regaining the erect posture. Eighteen months later he began to suffer from pins and needles sensation in the right arm; it became weak, and was no longer able to guide or grasp things properly. Numbness was complained of in the right leg and foot, the right hand, and left knee. The muscular sense was deficient in all four limbs. There were fibrillary and undulating tremors in the muscles of the limbs. He complained of occasional cramps in both legs; the latter were drawn up involuntarily at frequent intervals, and caused him much pain. He then lost power in all four extremities, so that he was absolutely helpless, and had to be fed. The urine occasionally

dribbled away of itself night and day for a week at a time, then the bladder would resume its normal functions for several weeks. About a year later he gradually recovered the power in the arms, and was able to feed himself once more. He then recovered power in the muscles of the trunk, so that he could sit up in a chair. Finally, the legs improved a little, so that he was able to move them about in bed. Dribbling of urine was very occasional If deprived of a water bed, a bed-sore threatened over the sacrum. The legs and feet gradually wasted and became drawn up, the toes becoming pointed. The knee-jerks and plantar reflexes were exaggerated for a time, and there was some ankle clonus. There was no further variation in the cord symptoms until his death from influenza.

Symptoms from fibromatosis of the cranial nerves.

There are isolated cases on record in which one or other of the cranial nerves was the seat of a tumour-like enlargement near its origin from the brain, so that it pressed on the latter and caused the ordinary symptoms of cerebral or cerebellar tumour. Loss of sight or of hearing has occurred in the rare cases in which the fibromatosis has involved the optic or the auditory nerve.

The symptoms arising from involvement of the cranial nerves outside the skull (which is much more common) do not differ from those related to tumours of the peripheral nerves. Mention has already been made of the frequency with which the vagus is affected in the neck, on one or both sides, and in the thorax or abdomen ; it is quite exceptional that this should be attended with any nerve symptoms ; attacks of difficult breathing, amounting to suffocation, and attacks of palpitation have been recorded, but it is not clear that these were always the result of the implication of the vagus in the fibromatosis. Tumour-like enlargements of the hypoglossal nerve have been known to interfere with the movements of the tongue and with mastication.

Symptoms from fibromatosis of the sympathetic nerves.

Considering the extent to which the main cords, ganglia, and plexuses of the sympathetic system may participate in generalised neuro-fibromatosis, it is at first sight remarkable that this should occur without giving rise to symptoms. The explanation is that the nerve fibres are just as capable of carrying on their important functions in spite of the fibromatosis, as are the fibres in the cerebro-spinal nerves. It is possible, however, that when the fibromatosis is generalised throughout the sympathetic system that it may be concerned in the failure of nutrition, amounting to cachexia, which is sometimes observed in the final stages of the malady and in the liability to succumb to intercurrent disease, *e.g.* tuberculosis, typhoid fever, influenza. There is no evidence to show that there is any connection between the lesion in the sympathetic nervous system and the abnormal pigmentation of the skin met with in many cases of generalised neuro-fibromatosis.

Symptoms from pressure on other structures and organs.

These are so rare as to be of little clinical importance. A large intercostal tumour has been known to press on the inferior vena cava and cause hydrothorax and ascites; the pressure of a tumour in the lumbar plexus on the common iliac veins has given rise to dropsy and thrombosis of the veins in the lower limbs; a sympathetic tumour has caused absorption of the bodies of the dorsal vertebræ; a tumour in the lumbar plexus has pressed on the ureter and caused frequent desire with partial inability to pass water, and hydronephrosis; tumours pressing on the recurrent laryngeal nerve and on the œsophagus have caused alteration in the voice and difficulty in swallowing.

Progress and terminations of generalised neuro-fibromatosis.

It is very difficult to estimate the progress in any given case of neuro-fibromatosis. Sometimes it is stationary, sometimes it is

progressive. In the majority of cases, however (apart from malignant transformation), the visible tumours have already attained their maximum size when they first come under observation, and they tend to remain stationary, and may continue so indefinitely. On the other hand, they may slowly increase in size, and new ones may appear, either singly or in crops, it may be in hundreds. The original tumours may involute to a certain extent, but they rarely disappear altogether, although I have seen the smaller subcutaneous tumours on the chest wall entirely disappear. Michet observed the disappearance of skin tumours, the area of the tumour remaining recognisable by a depression of the skin, and by insensibility to the prick of a needle.

The injurious influence of trauma, especially in the form of operative interference, has been repeatedly observed. Numerous cases are reported in which the patient attributed an increase in the size, and an exaggeration of the symptoms of a particular tumour to a blow; surgeons are familiar with the fact that the removal of one or more tumours by operation has been followed by greater activity and an apparent generalisation of the fibromatosis, exemplified by the appearance of fresh tumours in other parts of the body, and an enlargement of those which already existed. The same observation applies to tumours and to pigmentations of the skin.

The general health is usually unimpaired so long as the disease is stationary. Patients with multiple neuro-fibromata have been known to enjoy good health up to the age of sixty or more. When the disease is progressive, and gives evidence of becoming generalised throughout the whole peripheral nervous system, they are liable to pass into a condition of marasmus or cachexia, which has been called by French authors, the *third stage* of the disease. They lose flesh and strength and become anæmic; they cease to care for food; the fingers may become clubbed (apart from tuberculosis), their health

may be undermined by suffering and loss of sleep, or they may become apathetic, listless, resigned, not moving or speaking unless in answer to questions; the memory is impaired, and the mental faculties are dull; they may be sad, gloomy, and despondent. In a considerable number of cases there may be persistent vomiting and diarrhœa. Death ensues from exhaustion, or from such complications as paraplegia, bed-sores, etc., or from some intercurrent disease to which they are able to offer but little resistance. These include phthisis or some other form of tuberculosis (six cases), pneumonia (five cases), typhoid (five cases), tetanus, influenza, cholera, etc. (see Table on page 92).

Special reference must be made to the occurrence of sarcoma in the subjects of neuro-fibromatosis, for it is a well-recognised termination of the disease, and a common cause of death. Its pathological bearings have been discussed already under the heading of "secondary malignant neuroma." While it may develop without apparent cause, and it may be, in a tumour which has been absolutely stationary for many years, it is certainly more liable to follow upon injury or operative interference, especially when the latter has been incomplete, *i.e.* when a tumour has been only partially removed. The sarcomatous transformation of any tumour is indicated by the aggravation of the nerve symptoms, and by the usual accompaniments of malignant disease. The tumour increases in size, and becomes fixed to its surroundings and to the overlying skin; the pain is excessive, and may absolutely abolish sleep; thus in a case observed by the author it was barely relieved by injections of morphine amounting to fifteen grains in the twenty-four hours; the rapid onset of motor symptoms is also characteristic, *e.g.* agonising spasms of groups of muscles, going on to contracture, paralysis, and extreme wasting of the muscles. Stationary tumours in other parts of the body may assume similar malignant characters, and may grow with a rapidity which can only be described as extra-

ordinary. Visceral metastases are exceptional; evidence of their existence may be obtainable in the shape of marked dulness over one or both lungs.

The frequency of sarcoma in neuro-fibromatosis may be gauged from the facts given in the Table on page 92. It would appear to occur in over seventeen per cent. of the total cases recorded.

The diagnosis, prognosis, and treatment of neuro-fibromatosis.

A knowledge of the disease ensures easy diagnosis. The combination of tumours and pigmentation of the skin with tumours of the nerve trunks is pathognomonic. Where the nerve trunks alone are involved, there might be temporary confusion with other forms of multiple tumours, using this term in the clinical sense, *e.g.* lipomata, gummata, enlarged lymphatic glands. In the neck, tumour-like enlargements of the cervical sympathetic cord, or of the brachial plexus, have been mistaken for tuberculous glands; care must be taken not to explain away the nerve symptoms in such cases, as being of hysterical origin. Multiple tumours in the neck and axilla have been diagnosed as Hodgkin's disease; there is no real resemblance between the two.

The prognosis should always be guarded. While the disease may remain stationary for an indefinite period, and be compatible with fair bodily health, the probabilities are that sooner or later it will progress and become generalised and prove fatal; that the disease usually terminates in death may be reasonably inferred from what has gone before. It may be, however, that the striking appearances met with post-mortem, have led to a disproportionate number of the fatal cases being placed on record.

Treatment.—As is the case in many other rare and interesting diseases, there is no treatment beyond that concerned in relieving the symptoms and complications. The dangers of operative interference are not to be lost sight of. When relief is urgently sought on

account of agonising pain connected with one particular tumour, it may be necessary to disregard the dangers in question, but inasmuch as removal of the offending tumour has been so frequently attended with disastrous results, it might be wiser to resect a portion of the nerve at a higher level, or in the case of the extremities, to recommend amputation. Where there are indications of sarcomatous transformation, early and high amputation affords the only chance of recovery.

Special clinical features of the plexiform variety of neuro-fibromatosis.

The plexiform tumour is often recognisable at birth or in the earliest years of life. The sites which it commonly selects, its physical characters, and its frequent association with elephantiasis, have already been described. The skin over the tumour may appear normal, or may show a brown coloration, or it may be thickened and hairy, as well as pigmented. The sensation imparted to the examining fingers by the complexly convoluted nerve cords is so characteristic that it is unlikely to be mistaken for anything else. The tumour may grow at the same rate as the child, or it may remain stationary for an indefinite period, or it may take on a more active growth without any apparent cause. The deformity is the chief source of complaint; it is very little or not at all sensitive; spontaneous pain is exceptional. When situated, as it very commonly is, in the upper eyelid and forehead, it may hang down and cover the globe, and may lead to secondary changes in the eyeball and loss of sight. It is more uniformly innocent than the generalised disease in the trunks of nerves; operations for its removal are well borne, even when incomplete as they often are, owing to the prolongation of the convoluted nerve cords into the substance of muscles, around blood-vessels, etc. The skin is dissected off with difficulty. When situated in the scalp, they

are often found, like the dilated arteries of a cirsoid aneurism, lodged in grooves in the bone, or in actual gaps in the skull. Operations are undertaken chiefly with the object of removing an unsightly deformity. Malignant transformation is an exceptional occurrence in the plexiform tumour; it has been observed by von Winiwarter and by de Morgan, and it is attended by similar features and by similar disastrous results to those observed in the generalised disease in the nerve trunks.

Recorded Cases of Plexiform Neuro-Fibroma.

No.	*Observer.*	*Age.*	*Age at Onset.*	*Sex.*	*Situation.*	*Characters of Tumour— Association with other forms of Neuro-Fibromatosis.*	*Heredity.*
1	Billroth	6	birth	m.	temple and upper eyelid		
2	do.	18	birth	m.	temple, upper eyelid, orbit	tumour lobulated like molluscum	
3	do.	15	birth	f.	temple, upper eyelid, cheek	like a molluscum	
4	Bruns	28	birth	m.	temple and towards occiput	tumour lobulated like elephantiasis ; gap in temporal bone	
5	do.	33	birth	m.	temple and upper eyelid	tumour like elephantiasis ; multiple tumours of skin and nerve trunks	mother has mult. skin tumours; brother has plexiform n.f., No. 6.
6	do.	43	birth	m.	temple and upper eyelid	like elephantiasis	do.
7	do.	20	birth	f.	upper eyelid, orbit	elephantiasis of upper lid ; defect in roof of orbit	
8	Marchand	12	birth	m.	temple, upper eyelid, orbit,	like elephantiasis	
9	Rizzoli Barbieri	6	2	m.	eyebrow and upper eyelid		
10	do.	24	4	m.	temple and upper eyelid		
11	von Dessauer	42		m.	temple, forehead, upper eyelid, loin, and exostosis of iliac crest	like elephantiasis ; gap in frontal bone ; multiple fibromata and pigmentation of skin	
12	Socin	27	birth	f.	temple, upper eyelid, cheek	like elephantiasis	
13	Rapok	17	infancy	f.	upper eyelid		father has multiple plexiform tumours.
14	Bruns	48	birth	m.	forehead, upper eyelid	tumour in form of flaccid folds of skin ; hyperostosis of frontal bone ; multiple tumours of skin and of nerve trunks	
15	Labbe	20	1	f.	forehead, upper eyelid	like elephantiasis	
16	Schuster	14	4	m.	nose and cheek	pigmentation of skin ; multiple tumours of nerves	
17	Albert	27	birth	m.	nose, cheek, upper arm	pigmentation of skin : multiple tumours of nerves ; multiple angiomata	
18	Laroyenne	5		m.	cheek	pigmentation of skin	

Recorded Cases of Plexiform Neuro-Fibroma—*continued*

No.	*Observer.*	*Age.*	*Age at Onset.*	*Sex.*	*Situation.*	*Characters of Tumour— Association with other forms of Neuro-Fibromatosis.*	*Heredity.*
19	Bruns	10	1	m.	chin to occiput	soft pigmented folds of skin ; overgrowth of lower jaw ; pigmented moles of skin ; multiple fibroma molluscum	
20	Rapok	27	birth	m.	over lower jaw	multiple subcutaneous tumours (? neuro-fibromata)	
21	Marchand	8	5	m.	behind ear and parietal region		
22	Guersant	13	9	f.	behind ear	like elephantiasis	
23	von Dessauer	29	birth	m.	parietal region and behind ear	like elephantiasis, dragging down auricle ; gap in parietal bone	
24	Cartaz	11	birth	f.	behind ear	skin thickened ; tumour lobulated	
25	Herczel	10	6	f.	occipital region	pigmentation of skin ; elephantiasis of arm ; multiple tumours of nerve trunks	grandfather and mother have multiple tumours of skin
26	Leisrink	13	birth	m.	occiput, scalp, neck	pigmentation of skin	
27	Depaul Verneuil	19	birth	m.	neck	lobulated folds of skin, pigmented and hairy	
28	Christot	18	8	f.	neck	elephantiasis of skin, hairy in parts	
29	Volkmann	30		m.	neck from ear to clavicle		
30	do.	10	birth	m.	cheek and neck	skin over tumour pigmented and hairy	sister has similar tumour in same situation.
31	Arnozan	40	birth	f.	neck	tumour in area of extensive pigmented mole ; pigmentation and tumours of skin generally	
32	Köbner	21	birth	m.	lateral wall of thorax	pigmentations, angiomata, lymphangiomata, multiple neuro-fibromata and fibromata mollusca in distribution of brachial plexus	
33	Pomorski	28		m.	wall of thorax and pleural cavity (intercostal nerves)	pigmentations and tumours of skin ; multiple neuro-fibromata	
34	Lacroix-Bonnand	12	6	m.	back of shoulder	tumour in area of extensive pigmented mole	
35	Bruns	18	birth	m.	back, junction of dorsal and lumbar spine	skin over tumour pigmented and hairy ; pigmentation of skin generally ; multiple neuro-fibromata	grandfather and three brothers have multiple neuro-fibromata and skin pigmentations.

36	Lotzbeck Bruns	12	birth	f.	sacral region	tumour originated in area of large pigmented mole	
37	Czerny	26	birth	f.	back and buttock and right thigh	tumour of enormous proportions ; pigmentation of skin ; fibromata of cutaneous nerves and of lumbar and sacral nerves	grandfather, father, and others, have large fibromata mollusca.
38	Robin	45		m.	solar plexus		
39	Passavant	58		m.	perineum and scrotum		
40	Garel	25		m.	inner aspect of upper thigh		
41	Rose	young		f.	fold between buttock and thigh		
42	v. Winiwarter	36	birth	m.	upper arm and shoulder	skin thickened and pigmented over tumour ; diffuse fibromatosis of brachial plexus	
43	Jacquean	10		m.	upper eyelid and covering eye		
44	Bobrow	10	2	m.	neck and side of head	macroglossia same side of tongue	
45	Boccasso	10			tongue and below jaw		
46	Ramakus Vincent	16			right side neck and occiput	skin over tumour pigmented	
47	Rushton Parker	45	childhood	m.	upper eyelid, covering eye	molluscum fibrosum over body generally	
48	Kriege	5		f.	submucous tissue of cheek		
49	Do.	33	16	m.	forehead		
50	Finotti	29	childhood	m.	shoulder, axilla, upper arm	sensitive subcutaneous tumours over chest and body	
51	Herczel	9	7	m.	left brachial plexus	elephantiasis and pigmentation of left arm	
52	Alexis Thomson	16	14	f.	left small sciatic, back of thigh	multiple subcutaneous neuro-fibromata	
53	Hodsdon	17	9	f.	right median nerve, upper arm	pigmentation of skin ; multiple tumours of nerve trunks	
54	De Morgan	15	birth	f.	radial nerve in forearm	elephantiasis of hand	
55	Tietze	27	7	f.	left side of head above ear	multiple tumours of skin and nerve trunks	
56	Goldmann	54	youth	f.	intercostal nerve	pigmentation and tumours of skin ; tumours of nerve trunks	

The first 42 cases in this table are quoted from Bruns' paper in the Beitrage zur Klinischen Chirurgie, Bd. VIII.
Cases in this table presenting evidences of generalised neuro-fibromatosis will also be found in the table on page 92.

Special Clinical Features of Elephantiasis Neuromatosa or Pachydermatocele

The period of onset is the same as the plexiform type of the disease with which it is so frequently associated. One of its favourite seats is also the same, viz., the head and neck. It is also met with on the trunk and extremities in the shape of large lobulated or folded pendulous tumours. Less frequently, it involves one or both of the lower limbs in the form of a more diffuse elephantiasis like that resulting from disease of the blood or lymph vessels. Unlike the latter, however, the point of origin and the progress of the neuromatous elephantiasis are scarcely, if at all, influenced by gravity and the dependent position of the limb. The enlargement is present at birth, or appears in the earlier years of life ; it frequently originates in a brown spot or mole ; it increases gradually or by fits and starts, until when adolescence or adult life is attained, it may present the appearances shown in Plate XVI. Its general characters have been described at page 80. The patient may or may not be mentally deficient, and may or may not present other manifestations of neuro-fibromatosis, in the shape of pigmentations and tumours of the skin, plexiform tumours, or those of nerve trunks. There are no symptoms connected with the elephantiasis beyond its bulk and unsightliness; eczematous discharge, excoriation, and ulceration are the result of inattention to cleanliness. The clinical diagnosis of its neuromatous origin may be impossible, unless it coexists with other manifestations of neuro-fibromatosis. Amputation has been the usual treatment adopted in the diffuse elephantiasis of the lower extremity, and its results have been eminently satisfactory ; the subsequent progress of the patient will depend on the presence or absence of generalised neuro-fibromatosis. In one case recorded by Max Jordan, the patient, a girl of seventeen, died of general weakness ten months after amputation of the thigh.

The lobulated pendulous tumours, met with on other parts of the body may be removed by ordinary surgical means.

CHAPTER VII

GENERALISED NEURO-FIBROMATOSIS

Abstract of Cases which have come under the Author's Personal Observation.

1. *Multiple tumours of right lower extremity without any apparent general disease of the nerve trunks; the tumours sensitive and giving rise to shooting pains; removal of the tumours; recovery.*

G. D., fifty-six, mason, Dundee, married, admitted 21st January 1898 to the University Clinical Wards, Royal Infirmary, Edinburgh, under the care of Professor Annandale. He has eight of a family, of which one son, aged thirty-two, has painless lumps in his buttock. About twenty-eight years ago he had a severe attack of sciatica in the left side. He has from time to time suffered from facial neuralgia. About thirty-three years ago he discovered a small lump, the size of a pea, in the right gluteal region, which at times was very painful. Eighteen years ago he discovered another small lump on the outer aspect of the leg, midway between the knee and the ankle, which has been the source of almost constant pain. About four years ago he discovered a nodule the size of a pea over the outer ankle bone, his attention being directed to it, as to the others, by pain. More recently, these lumps have all increased in size, and have caused him much suffering.

The patient is a strong healthy man. He exhibits the following tumours:—(1) One as large as a pigeon's egg in the right buttock in the position of the small sciatic nerve; when compressed, *e.g.*

by sitting upon it, pain shoots down the back of the thigh, and into the perineum. (2) A slightly smaller lump about the middle of the antero-lateral aspect of the right leg, in the position of the museulo-cutaneous nerve ; it gives rise to a good deal of pain, which shoots up the leg and down to the foot, the latter feels dead and cold ; in addition to these spontaneous pains, the leg feels sore and tired after walking, and on jarring the foot the pains shoot up the leg as far as the tumour. (3) A rounded tumour like a marble over the right external malleolus, which is very freely movable, and not at all tender, even when pressed upon by the boot. If related to a nerve, it must be to a branch of the external saphenous. There are no other tumours, and the accessible nerve trunks appear normal.

On the 28th January 1898 all three tumours were exeised by Professor Annandale without differentiating or interfering with the nerves with which they were connected. The relief from pain was complete and permanent so far as the buttock was concerned. I heard from him sixteen months later to the effect that the leg still troubles him owing to "burning sensations running from where the tumour was removed from the leg down to the toes," and "a sort of creeping pain as if something were running up and down the leg."

The sciatic tumour measured 6 cm. in length, and 2·5 cm. in breadth ; it had a smooth capsule which was adherent at one point to the gluteus maximus ; on section it was very soft, friable and granular. The museulo-cutaneous tumour measured 2 cm. in length, and 1 cm. in breadth ; its capsule was also adherent to the adjacent muscle (peroneous longus ?). The external saphenous tumour was spherical, and about 1 cm. in diameter.

2. *Plexiform neuroma of the left small sciatic nerve, and multiple subcutaneous neuro-fibromata on the trunk and limbs. Partial removal of the plexiform tumour. Continued good health and freedom from symptoms three and a half years later.*

C. J. M., sixteen, schoolgirl, Ross-shire, admitted to the University Clinical Wards, Royal Edinburgh Infirmary, 10th October 1892, under the care of Professor Annandale. She belonged to a healthy family, and was herself a fairly nourished, active, intelligent girl. Her complaint was of a swelling on the back of the left thigh, which was noticed accidentally two years ago, it being at that time about the size of a walnut; it had never caused her any pain or other discomfort; she was not aware of the existence of any other tumours.

The tumour complained of was found to occupy the posterior and inner aspects of the left thigh, from a finger's breadth below the fold of the buttock downwards for 16 cm. From side to side it measured 14 cm. The overlying skin was normal in appearance, and moved freely upon the tumour. The tumour itself moved with the hamstring and adductor group of muscles; on palpation it was quite insensitive, and felt like a mass of hard worms, or convoluted knotted cords; it had no defined margin, for the cords of which it was composed could be traced into the surrounding tissues in all directions. By those who examined the tumour, it was regarded as being unlike anything with which they were familiar.

On further examination the following tumours were discovered:— A nodulated mass similar to that above described filling up the left popliteal space, bulging from it and extending downwards as far as the middle of the calf. A longitudinal series of minute subcutaneous tumours on the anterior aspect of the left thigh in the line of the femoral artery in Scarpa's triangle (crural branch of genito-crural

nerve); another series on the outer aspect of the left thigh, extending from a hand's breadth below the great trochanter, as far as the level of the patella (branches of external cutaneous nerve); a limited number of similar pea-like tumours beneath the skin, covering the subcutaneous surface of the tibia (branches of internal saphenous nerve). In the right thigh, a few scattered, isolated, pea-like, subcutaneous tumours along the back of the thigh and popliteal space (small sciatic nerve), and two longitudinal series on the anterior aspect of the thigh, one in the line of the femoral vessels in Scarpa's triangle (crural branch of genito-crural nerve), the other on the inner aspect of the thigh, as far as the internal condyle of the femur (branches of internal cutaneous nerve). In the right arm there was one subcutaneous nodule like a split-pea, one inch below, and to the inner side of the centre of the bend of the elbow (anterior branch of internal cutaneous nerve). The left arm was exempt. In the abdominal wall there were a number of scattered, subcutaneous, pea-like nodules between the umbilicus and the iliac crest on either side (anterior branches of lower intercostal nerves). The accessible nerve trunks were apparently normal. None of the tumours, including the large plexiform variety in the left thigh, were the seat of any pain, nor were they in the least sensitive to pressure. As regards their distribution, it will be noted that with the exception of the plexiform tumour, which involved the small sciatic, all the others affected the purely cutaneous nerves of the abdominal wall, of the right upper, and of both lower limbs.

Professor Annandale operated upon the plexiform tumour on the 19th October 1892, making a mesial incision along the back of the thigh through the skin and fat; the tumour tissue which was then exposed appeared like strings of boiled tapioca, partly accumulated into a central mass, partly in the form of isolated tortuous cords radiating out from the margins of the latter, and sprouting through the deep fascia (fascia lata) into the fat beneath it, and penetrating also the substance of the subjacent hamstring and adductor muscles.

The greater part of the tumour was removed, but no attempt was made to follow out its ramifications.

The patient returned to her home, where she was seen thirteen months later by Dr Murray Leslie, who kindly furnished the following report:—"The patient has enjoyed the best of health since leaving the Infirmary; she has grown considerably, and has gained 7 lbs. in weight; she has commenced work in the telegraph office; the tumour mass on the back of the left thigh, which was still to be felt after the operation, has not appreciably altered since then; it is a little tender to the touch, and there are occasional pains shooting down the knee. The other tumours are in *statu quo* and give rise to no pain." Two and a half years later (30th July 1896) she was again seen by Dr Leslie, who reported that she was now in better health than she had been for years, and that the plexiform tumour in the thigh had not altered in any way.

The portion of plexiform tumour removed (Plate XI.) measured 14 cm. in length, 10 cm. in breadth, and 5 cm. in thickness. It was made up of a series of convoluted and beaded cords, of a soft, gelatinous, almost translucent tissue, held together by loose areolar fat. The different strands were easily separated from each other, and then exhibited an irregular plexiform arrangement. On the superficial aspect of the tumour, the strands extended up to the deeper layers of the skin; on the deep aspect they pierced the fascia lata and hamstring muscles. The microscopic examination was incomplete, as the specimen was not preserved in Müller's fluid. Transverse sections were made of the strands of the tumour, and were stained in hæmatoxylin and eosin; the nerve fibres were so few in number that they were only discovered after very careful search, lying chiefly at the periphery of each strand in small groups; the numerous blood-vessels had a delicate but distinct wall. The general tissue of the tumour was derived from an overgrowth of the endoneurium of the small sciatic nerve.

The preceding case is a typical one of plexiform neuro-fibroma in combination with multiple tumours in the course of the cutaneous nerves; the plexiform tumour pursued an innocent course in spite of operative interference, and persisted indefinitely in a quiescent condition, having apparently reached its acme of development.

3. *Plexiform neuro-fibroma of the right median nerve in the upper arm; multiple neuro-fibromata of the upper arm and hand; punctiform and patchy pigmentation of skin; removal of plexiform and some of the nerve trunk tumours; recovery.*

J. M., dressmaker, seventeen, Perthshire, admitted to the University Clinical Wards, Royal Edinburgh Infirmary, 30th November 1898, under the care of Professor Annandale. She belonged to a healthy family, and had had no previous illnesses. A tumour on the right upper arm was first noticed eight or nine years ago; since then it has gradually increased in size; there have been occasional pains down the arm, but they were not severe enough to keep her awake at night. On admission she was found to be a well-nourished, dark-haired girl, of a mental calibre rather above the average for her age and circumstances. She presented a series of tumours and of pigmentations of the skin having the following characters:—

Tumours.—(1) A large visible tumour on the inner aspect of the right upper arm, extending upwards into the axilla towards the coracoid process, and downwards beyond the middle of the upper arm nearly to the bend of the elbow; it was slightly tender on pressure, and was felt to be made up of a number of knotted cords and lumps connected with one another. It was not adherent to the overlying skin. (2) A series of small nodules, like almonds, in the line of the median nerve in the left upper arm. (3) A well-defined almond-shaped tumour in the substance of the ball of the left thumb in its inner half, of hard consistence, and occasionally tender

on pressure. (4) An elliptical tumour, almost as big as a pigeon's egg, in the palm of the left hand in the interval between the fourth and fifth metacarpal bones (branch of ulnar nerve).

Pigmentations.—These are scattered all over the body ; they vary in colour from a pale coffee brown to black, and in size from a pin point to areas measuring 2·5 by 5 cm. ; the pigmentations are accompanied by a considerable growth of soft hair, except on the abdomen. They are most numerous on the back, but there are a few on the face, and on the arms and legs.

Mr Hodsdon, who operated upon the plexiform tumour on the 7th December 1898, kindly supplied me with the following statement. Having reflected the skin, which was not connected with the tumour, the biceps was found displaced outwards, and the ulnar nerve and brachial artery inwards and backwards, while the median nerve passed through the centre of the tumour ; the latter, which presented the usual appearances of a plexiform tumour, was dissected out in two portions to avoid damaging the median nerve. It was adherent in parts to the periosteum of the humerus. The median and ulnar nerves themselves were very greatly and irregularly thickened, several nodules as large as filbert nuts being shelled out from their sheaths. The operation was not followed by any disturbance of function, beyond the appearance the following day of two or three small blisters on the ulnar side of the little finger.

The naked eye appearances of the masses removed at the operation were those characteristic of the plexiform neuro-fibroma. A small portion of the tumour unravelled by dissection is shown in Plate XII.

Microscopically, each individual strand was found to consist of one bundle of nerve fibres surrounded by the perineurium which formed the external investment or sheath ; the entire bulk of the strand was composed of the overgrown endoneurium ; the sharp definition between the perineurium and endoneurium was lost, the

two merging into one another. The nerve fibres showed a remarkable degree of dissociation; although on the whole more numerous towards the periphery of the strand, they were also found scattered throughout its substance (Plates XIII. and XIV.). They did not appear to have undergone degeneration.

4. *Multiple fibromata of the nerve trunks and skin, the former causing much suffering; excision of certain tumours; relief from pain; recurrence of tumours, and development of fresh ones in different parts of the body; cachexia; death.*

T. C. M., twenty-five, bookseller, Edinburgh, was admitted to the University Clinical Wards, Royal Infirmary, Edinburgh, 3rd January 1893, under the care of Professor Annandale, complaining of painful lumps in the neck, arm and leg. Belonging to a healthy family, he had always been healthy until quite lately, when he began to lose flesh and strength, so that he had to give up work about a month ago. He first noticed the lumps, of which he specially complains, about seven years ago; he cannot say in what order they appeared, but thinks they came simultaneously. At first they gave him no trouble, but he soon noticed that many of them were painful when handled or knocked, and that the pains persisted for some hours thereafter. They have increased in size very slowly. Two of the smaller skin tumours were removed by his own doctor eight months ago. During the last five months the tumour in the left upper arm has given him almost continuous pain, so severe during the night as to interfere with sleep; the pain is further aggravated by use of the arm and by injury. He is quite certain that no fresh tumours have developed during the last three years. He is an intelligent, well-educated man, much reduced by pain and sleeplessness. His internal organs and functions appear

to be normal. There is marked clubbing of the fingers. His tumours may be described in two groups, those belonging to the skin itself, and those obviously related to nerve trunks.

(1) *Cutaneous tumours.*

These exactly correspond in appearance to what are commonly called soft fibromata of the skin ; they vary in size from a pea to a walnut ; they are spherical and semi-pedunculated, or flattened and sessile ; they are situated in the skin itself, and move with it ; they are definitely circumscribed, soft, flaccid, compressible, and not at all sensitive. There are nine of these tumours scattered over the trunk and limbs ; most of them are situated in the area of well-known cutaneous nerves, as follows :—

1. In the centre of the right infraspinous fossa (circumflex nerve).
2. Over the middle of the sacrum (posterior division of sacral nerves).
3. In the loin immediately above the right iliac crest (posterior divisions of lumbar nerves).
4. Two inches above the right trochanter (external cutaneous nerve).
5. In the centre of the anterior aspect of the left upper arm (internal cutaneous nerve).
6. At the bifurcation of the median vein below the bend of the left elbow (internal cutaneous nerve).
7. Over the median basilic vein at the left elbow (internal cutaneous nerve).
8. Over the posterior border of the deltoid muscle, close to its insertion (circumflex nerve).
9. Over the centre of the anterior aspect of the left clavicle (supra-clavicular nerves).

(2) *Tumours related to the trunks of nerves.*

These are subcutaneous or subfascial tumours, very sensitive on handling, and when pressed upon, cause intense pain which shoots along the peripheral distribution of the nerve involved. They vary in size, but on the whole are larger than the skin tumours, and are apparently firmer in consistence. While some of them are of even contour and elliptical shape, some are lobulated or annulated at right angles to their long axis. They can be moved with some freedom from side to side, but not longitudinally. No record was kept of the total number of tumours, but the following are the more important, being those specially complained of:—

1. Involving the internal cutaneous nerve in the left upper arm; this tumour measures 6·5 cm. in length by 3 cm. in breadth; although in the main elliptical, it is crossed by a series of deep transverse furrows; it has caused him more pain than all the others put together; the pain starts in the tumour and shoots down the forearm. It is extremely sensitive.

2. Involving a lateral branch of the third intercostal nerve, between the left scapula and the spines of the vertebræ (4·5 × 3·2 cm.). It is lobulated and slightly sensitive.

3. Involving the descending branches of the cervical plexus in the posterior triangle of the neck on the left side (6 × 3 cm.). It is slightly sensitive.

4. Involving the great sciatic nerve in the middle of the right thigh, underneath the hamstrings (15 × 6 cm.). It is at the same time the largest and the least sensitive of all the tumours. Pain is felt in the tumour when the sciatic nerve is pressed upon in the buttock.

5. Involving the external popliteal nerve where it crosses the neck of the right fibula; it is elliptical and extends some 7 cm. in the long axis of the nerve; it is very sensitive, and much

exposed to injury; the pains shoot down the front of the leg to the toes.

At the request of the patient to be relieved of his sufferings, Professor Annandale removed the nerve trunk tumours on the 11th January 1892, excepting those in the posterior triangle of the neck and in the back of the thigh. The tumour of the external popliteal nerve was removed along with a portion of the nerve above and below; the others were shelled out from their capsules; they all consisted of a similar translucent or gelatinous greyish-white soft solid tissue. The tumour in the skin over the left clavicle was also removed for investigation. The external popliteal nerve, where it was cut across at the operation, was thicker than normal, and showed a moderate degree of fibromatosis; the other accessible nerve trunks did not appear to be thickened. The wounds healed rapidly; the patient was relieved from pain; there was drop-foot from paralysis of the external popliteal, but practically no anæsthesia. He was discharged from hospital and lost sight of.

Twenty-two months later, I saw the notice of his death in the newspaper. On inquiry I discovered that after leaving the hospital he had lost strength and flesh, that tumours had recurred in the position of certain of those which had been excised, and that numerous fresh growths had developed in different parts of the body. A specially large tumour had appeared in the left axilla. The tumours were soft or semi-fluid in consistence, and grew with a rapidity like that of the most malignant sarcomata. He became extremely emaciated. An area of dulness developed in the upper lobe of the left lung, and there was difficulty in swallowing. His own doctor, who was not aware of what had been observed in the Infirmary, diagnosed the case as one of Hodgkin's disease. A sectio was not obtained. From the progress and termination of the case, there can be no doubt that the cause of death was sarcoma, which had become disseminated from one of the original tumours, the latter

having undergone sarcomatous transformation ("secondary malignant neuroma").

The microscopic appearances of the tumours and nerve removed at the operation were as follows :—Transverse sections of the external popliteal nerve above the tumour showed typical and pronounced fibromatosis of the endoneurium within the primary bundles ; of the eleven bundles which constituted the entire nerve trunk, only one had entirely escaped ; the others were all affected to a varying degree ; the overgrowth of the endoneurium was for the most part evenly distributed throughout each bundle, so that the nerve fibres were individually isolated or dissociated. The tumours themselves, being made up of overgrown endoneurium, presented the structure of the latter, rather than that of any type of tumour. There was a gradual transition between the tissue of the so-called tumour and the perineurium or capsule of the tumour. There was absolutely nothing in the structure of these primary tumours to suggest the likelihood of recurrence or of sarcomatous transformation.

The cutaneous tumour from over the centre of the left clavicle presented several interesting features ; instead of being, as in an ordinary skin fibroma, a uniform mass of newly formed fibrous connective tissue, it exhibited the normal structures of the skin, *i.e.* fat lobules, sweat glands, blood-vessels, etc., permeated and studded with nerve twigs, of which the great majority were in a condition of fibromatosis, in consequence of which they were very greatly thickened ; here and there the fibromatosis was exaggerated into actual tumour nodules or neuro-fibromata. The medullary sheaths of the nerve fibres being stained dark blue, I was able to trace them in their course through the true skin, and identify the fibromatosis and tumour nodules related to them ; otherwise, one might have regarded the latter as related to the sheaths of the smaller arteries, which they frequently accompany, or to the sweat glands. Neither

the blood-vessels nor the sweat glands were altered in any way, although the former were abnormally numerous, and in the deepest layers of the skin or base of the tumour they were dilated into large venous sinuses, filled with blood, like those in a cavernous angioma. The nerve bundles, which as already indicated were almost universally the seat of fibromatosis, were cut in various directions, some longitudinally, some transversely. It was not possible to trace the nerve fibres beyond the coils of the sweat glands, as the epidermis and papillary portion of the skin were absent from the sections successfully stained by the Weigert-Pal method.

There was no evidence of any degeneration of the nerve fibres themselves. From the appearances above described, it is evident that what was observed clinically as a projecting tumour of the skin was not really a tumour at all, but a localised fibromatosis of the cutaneous nerves, together with dilated blood-vessels. There was no fibromatosis or other alteration in the sweat glands or other appendages of the skin.

5. *Multiple neuro-fibromata, one of which, involving the median nerve, caused great suffering; excision of tumour of median nerve; recurrence as sarcoma; amputation through upper arm; recurrence in stump; amputation at shoulder joint; recurrence; development of sarcoma in left lumbar plexus; cachexia; death.*

Allan Brash, twenty-eight, labourer, unmarried, admitted to the University Clinical Wards, Royal Infirmary, Edinburgh, 30th July 1894, under the care of Professor Annandale, complaining of a painful tumour of the right arm. His family history was free from taint. He had always been healthy, with the exception of an attack of inflammation of the bowels at the age of sixteen. At the age of

thirteen, before he left school, he noticed a lump on the left temple. Eleven years later, at the age of twenty-four, he noticed a lump on the right upper arm; this slowly increased in size, but for three years gave him no trouble; he then began to suffer from pains, and of "pins and needles" sensations down the arm. More recently he noticed a lump on the left arm. He is a spare, dark-complexioned man, of mental calibre considerably below the average. His general health is fair. He sweats readily and profusely. He does not sleep well on account of the pains in the right arm. Scattered widely over the head, trunk and limbs, there are innumerable tumours beneath the skin and along the course of the nerve trunks, varying in size from the head of a pin to the egg of a goose. A limited number of the subcutaneous tumours are painful and sensitive on handling; these, along with the prominent painless tumour over the left temple, are the only ones known to the patient. The main nerve trunks of the limbs, apart from the tumours, are sensitive to pressure, and he winces, and occasionally jerks the limb involuntarily.

Distribution and characters of the tumours.[1]

Head and neck.—In the left temple there is a soft, hemispherical subcutaneous tumour, freely movable and quite insensitive (3·5 cm. in diameter) involving the temporal branch of the temporo-malar nerve. There is a chain of minute pea-like nodules behind and on a level with the left ear in the line of the small occipital nerve. In the posterior triangle of the neck on both sides there are a number of small tumours, and a larger one, the size of a pigeon's egg, all of them soft, freely movable and insensitive, and corresponding to the distribution of the clavicular branches of the supra-clavicular nerves. There is a similar series over the shoulder on both sides, corresponding to the acromial branches of the same nerves.

[1] In recording the facts of this case, I derived valuable assistance from Mr Elmes, clinical clerk.

Trunk.—There is a numerous and fairly symmetrical series on the posterior, lateral, and anterior aspects of the trunk, from the level of the nipples downwards, following generally the distribution of the intercostal nerves. The linea alba is exempt, and there are few in its immediate neighbourhood. The majority are on the lateral aspects of the trunk, in the spaces between the ribs; a limited number lie upon the ribs. They are relatively scanty over the back, and are irregularly distributed from the vertebra prominens to the cleft of the nates. Some of them are close to the middle line, one as large as a bean lying over the first sacral vertebra.

The above tumours are subcutaneous or more deeply placed; they are quite insensitive, many of them are elongated, and are arranged in chains in the long axis of the intercostal and lumbar nerves.

Extremities.—In both upper extremities there are longitudinal series of small, subcutaneous, insensitive tumours in the line of the circumflex nerve over the deltoid, in the line of the cutaneous branch of the musculo-spiral nerve in the groove between the biceps and supinator longus muscles, and in the line of the internal cutaneous nerve on the inner aspect of the upper arm. The hand and fore-arm are exempt, save a small nodule like the head of a pin about the middle of the dorsal aspect of the fore-arm. About a hand's breadth above the internal condyle of the right humerus, there is a large (8 × 8 cm.) tumour of the median nerve, which is the seat of spontaneous pain, and is extremely sensitive to pressure; the pain shoots down the fore-arm to the wrist and fingers; the overlying skin is stretched but can be lifted from the tumour, the latter is lemon-shaped and apparently solid. It was on account of this tumour that the patient applied for treatment. There is a tumour the size of a plum in the corresponding situation in the left arm; it is freely movable and insensitive.

It will be observed that the tumours of the upper extremities are remarkably symmetrical.

In the lower extremities, there are longitudinal series of minute, subcutaneous, insensitive nodules along Poupart's ligament, along the line of the femoral artery, and over the gracilis muscle. The remainder are larger and more deeply placed tumours in the position of the anterior crural and sciatic nerves on the right side. One of these, as large as a hen's egg, is situated beneath the outer half of Poupart's ligament; it is movable and very sensitive. A second, the size of a walnut, is in the line of the sciatic nerve, just below the fold of the buttock, and a third in the same line, also the size of a walnut, in the upper part of the popliteal space. The sciatic tumours are but little sensitive.

The above description embraces one hundred and twenty-four tumours; there were doubtless as many more scattered throughout his body, which did not reveal themselves on clinical examination. There was no alteration in the motor or sensory functions, apart from the pains.

Being in charge of the wards in the absence of Professor Annandale, I operated upon the tumour of the right median nerve on the 7th August 1894. After exposing it by a free incision, the median nerve was found to be very greatly thickened above, and still more below the tumour; in the latter position it was beaded, and as thick as a finger. The capsule of the tumour (or general sheath of the nerve) was incised, and the greyish translucent tissue composing it was shelled out; the removal was not quite complete owing to disinclination to damage the nerve fibres lying behind the mass. Professor Terrier of Paris, who happened to be present, regarded it as malignant. The pains disappeared, the wound healed, and the patient went home.

The tumour was elliptical, measured 5·5 × 4 cm.; its exterior was smooth and shining; on section, the peripheral portion was firm, fibrous and fasciculated; in the centre it was more gelatinous and semi-fluid, of a grey yellowish white colour, with areas of brown

pigmentation. Microscopically the tumour was composed of the same overgrowth of endoneurium as has been described in the preceding cases; in the central portions, the cells had almost entirely disappeared (as a result of myxomatous degeneration ?), leaving nothing but the open fibrillar network of the original tissue; nearer the periphery, there was the usual typical structure; at one point, however, there was a decided transition to a more cellular and more tumour-like tissue of the spindle-celled or myxo-sarcoma type; this transition could be traced step by step from the branching cells of the endoneurial connective tissue. The blood-vessels throughout the tumour had very thin walls.

Clinical history continued.—The microscopic appearances described made a recurrence of the growth a likely event. The patient returned four months later, stating that the pains had reappeared in connection with the tumour of the arm; the latter was as prominent and as sensitive as it had been before the operation; it was adherent to the scar and to the surrounding tissues, and at one point was fungating and bleeding on the surface. The hand was almost useless, whether from the pain, or from partial destruction of the nerve by the growth, it was impossible to say. As the tumour was growing rapidly, and was evidently sarcomatous, Professor Annandale amputated through the upper arm on 18th January 1895. All the nerves of the limb presented an extreme degree of fibromatosis; the cut surface of the muscles showed white fibrous nodules in their substance. The stump healed rapidly, and he went home in apparent good health.

Dissection of the amputated arm.—All the cutaneous nerves as far as the bend of the elbow, showed series of small elliptical tumours; the anterior cutaneous branch of the ulnar showed two elongated swellings, one about the middle of the forearm, the second immediately above the wrist. All the main trunks, where divided in the amputation, were characteristically enlarged, beaded, and of wavy

contour; the thickening was greatest in the ulnar and in the internal cutaneous nerves, which measured respectively 10 mm. and 12 mm. in diameter; it was least in the musculo-spiral. Below the level of the elbow joint, all the nerve trunks were normal. The median nerve which was the seat of the recurrent sarcoma, was moderately thickened above the tumour, while below, it suddenly bulged into a glistening encapsulated tumour, the size of a walnut, occupying the bend of the elbow. The recurrent tumour itself infiltrated the skin and other contiguous tissues; it was greyish-pink on section, and somewhat friable in consistence. Microscopically, it was composed of spindle cells of moderate size; the blood-vessels were merely chinks or spaces between the cells of the tumour. There were no peculiarities to indicate its origin from a nerve sheath.

Clinical history continued.—Ten months after amputation of the arm, he began to have pain in the stump which became enlarged from return of the growth. Although the latter grew rapidly, he allowed another month to elapse before presenting himself at the hospital. By this time the tumour had attained a considerable size; it was excessively tender, and the overlying skin was tense and red.

In the absence of Professor Annandale I amputated at the shoulder joint (17th December 1895) by a highly placed anterior racket incision; the muscles were divided at the base of the flaps; there was difficulty in securing the axillary artery from the way in which it was buried amongst the greatly enlarged and bulbous nerve trunks. The wound healed rapidly, and he left the hospital in apparent good health. The recurrent growth was a perfect type of spindle-celled sarcoma. He was re-admitted six months later with a large number of secondary tumours in the region of the shoulder stump, and beneath the great pectoral muscle; many of these were freely movable, and felt like enlarged glands.

His general condition had greatly deteriorated; he was able to

take very little nourishment, and could not sleep for pain. Apart from the malignant tumours in the region of the shoulder stump, there was an evident increase in size and sensitiveness of all the accessible nerve trunks, and of the tumours related to these. Certain tumours which had been observed as insensitive at the time of his first admission to hospital, were now very sensitive indeed. The pains were so severe, especially in relation to the left lower extremity, that he required an injection of morphine every two or three hours. He had as much as fifteen grains in the twenty-four hours. The whole left lower extremity was so sensitive that the least touch made him cry out, even when under morphine; he maintained it in an attitude of acute flexion at the hip and knee joints; he could not straighten it himself, and the least attempt to extend it pained him severely, and it was drawn up again in a condition of spasm or cramp. The condition of the knee jerk could not be determined. In the intervals between the more severe pains he had the sensation of "pins and needles," especially in the region of the thigh and knee joint.

This condition of the left lower limb was associated with the presence of a large tumour, which was easily felt in the position of the left psoas muscle, and which was evidently a sarcoma involving the cords of the lumbar plexus, and pressing on the ureter, for there was constant desire to pass water, but frequently inability to do so.

The right lower extremity moved freely without pain; the individual nerve tumours were sensitive; compression of the large tumour of the anterior crural beneath Poupart's ligament caused jerking of the quadriceps muscle. There were occasional painless cramps of the left arm, from the elbow down to the fingers, during which the fingers became spread out in a stiff claw-like attitude. On the trunk the subcutaneous nerve tumours had increased in size and number. On the forehead a series of small nodules had recently appeared in the line of both supraorbital nerves.

At intervals he became very noisy and excited, so that he had to be isolated; as the morphine seemed to aggravate these attacks it was discontinued, after which he became quite sensible again, and said the pains had disappeared. The recurrent tumour in the shoulder stump had attained the size of a child's head, and had fungated through the skin. He was taken home at his own request, and died peacefully of exhaustion on the 25th October 1896, a little more than two years from the first operation.

Post-mortem examination.—This was made under difficulties on the afternoon of the same day, with the assistance of Dr J. H. Balfour of Portobello. The body was reduced to a skeleton. There was dropsy of both feet. All the visible tumours related to the trunks of nerves had undergone considerable diminution in size; there were no visible (secondary) sarcomatous growths in the viscera. There was a large sarcomatous mass, as big as a child's head, involving the left lumbar plexus, the left psoas muscle, and the adjacent bodies of the lumbar vertebræ; the latter were infiltrated and softened, so that they broke down under the finger nail; the tumour displaced the left kidney upwards, compressed the left ureter and left common iliac vein; it was prolonged along the psoas muscle and anterior crural nerve as far as Poupart's ligament. The inferior vena cava and both common iliac veins were obliterated by thrombosis of old standing. All the muscles exposed in the dissection showed spindle-shaped white masses in their substance in the lines of the nerves. The nerve plexuses in the subserous coat of the stomach, and at the bifurcation of the aorta, were evidently the seat of fibromatosis, and were removed along with the nerves of the extremities, etc., for further examination. Inspection of the brain and spinal cord was unfortunately not permitted.

The cerebro-spinal nerves showed wide variations in the degree and distribution of the fibromatosis; so far as could be observed, no nerve, whether large or small, whether motor, sensory, or mixed in

function, was altogether exempt from the change. In illustration of the naked eye appearances of the main nerve trunks of the limbs, a description will be given in the first place of the left sciatic nerves, and of the right anterior crural nerve, as typical of the changes presented by all the nerves of the extremities.

The left great sciatic nerve (Plate III.) is enlarged throughout, it is flattened from before backwards, and measures 2·5 cm. × 1·5 in transverse section. Its external surface presents numerous localised elliptical bulgings or projections corresponding to local exaggerations of the fibromatosis in individual nerve bundles at the periphery of the nerve trunk. Its main divisions are similarly enlarged and nodulated, the internal popliteal being nearly as thick as the finger; the external popliteal is smaller, but is more nodulated, so that it resembles a rosary. The various small branches, both of the main trunk, and of its two terminal divisions, are more enlarged than the trunks themselves, and are more irregularly beaded. The small arteries entering the great sciatic are abnormally large.

The small sciatic nerve is irregularly thickened and beaded, as are also the minute branches arising from it.

The right anterior crural nerve (Plate IV.), at the level of Poupart's ligament is so greatly thickened that it measures 2 cm. from side to side, and 1·1 cm. from before backwards. A little lower down where it breaks up into a leash of branches there is a considerable amount of inflammatory adhesion and matting of the branches to each other. There is a large (6 × 4 cm.) egg-shaped tumour belonging to quite a small branch, the nerve fibres of which are spread out upon one aspect, and are gathered together again beyond the tumour, whence they run down the thigh as an ampullated cord. The other branches of the main trunk, both cutaneous and muscular, are represented by thickened ampullated cords; there is no variation in the amount and degree of the fibromatosis corresponding to differences in function; the

motor branches on entering the muscles present, if anything, an exaggeration of the fibromatosis, which enables one to trace in the substance of the muscle minute nerve filaments which would otherwise be invisible to the naked eye. The appearances of the cross sections of the above nerves are those of a series of fibrous bundles of very unequal size, loosely held together, and invested by the general epineurium. The microscopical appearances of the nerve trunks have been already described.

The large subcutaneous tumour over the left temple (which measured $2{\cdot}3 \times 1{\cdot}7$ cm.) was simply an encapsulated mass of overgrown endoneurium, in which no nerve fibres could be identified; a second smaller tumour was situated immediately beneath it, and below the latter a minute nerve trunk was the seat of a moderate degree of fibromatosis. This nerve trunk was a branch of the fifth nerve (temporal branch of temporo-malar) distributed to the temple.

The skin and subcutaneous tissue throughout the body, although not visibly altered on the surface, is studded with innumerable small tumours or fibrous nodules in relation to the cutaneous nerves, which were also affected with the fibromatosis. They vary in size from nodules which are only to be seen with the microscope up to the size of small peas, 2 to 5 mm. in diameter. They are more numerous below the level of the sweat glands; those in the vicinity of the latter are quite distinct from them. Nerve filaments altered by fibromatosis can be traced into the fibrous nodules. In addition to the circumscribed nodules or tumours, there is a more diffuse fibrosis of the whole skin, extending from the paniculus adiposus right up to the surface epidermis, with fibromatous nerve filaments running through it in all directions.

Intramuscular neuro-fibromatosis.—At the different amputations, and at the post-mortem examination, the cut surfaces of all the muscles showed white nodules or tumours between the muscular

fibres; elliptical in longitudinal section, and rounded in transverse section, they varied in size from what can only be seen with the microscope, up to visible tumours as large as hazel-nuts; microscopically all the nerve filaments within the muscles showed an extreme degree of fibromatosis, and there were all transitions, from the altered nerve filaments up to the visible tumours. Within the latter, very few, scattered, and imperfectly stained nerve fibres may be seen, dissociated from one another in the usual way.

At the first amputation through the arm, the muscle fibres themselves were quite healthy, except in the immediate vicinity of the larger tumours, where they were somewhat flattened and compressed.

Cranial nerves.—The trigeminal and vagus are the only cranial nerves of which there is any record. Reference has already been made to a large subcutaneous tumour and to the existence of fibromatosis in the temporal branch of the temporo-malar nerve on the left side. The left vagus was the seat of an egg-shaped tumour at the level of the cricoid cartilage, measuring 2 cm. in transverse section. The microscopic appearances have been described and illustrated in Chapter IV., page 59.

Sympathetic nerves and ganglia.—The carotid plexus which is described as belonging to the sympathetic system, and as containing a certain proportion of medullated nerve fibres, was also affected with a moderate degree of fibromatosis; the overgrowth of endoneurium was much more cellular than in the average cerebro-spinal nerves, and it was much less sharply defined from the surrounding connective tissue; *i.e.* the special perineurium does not exist. No ganglion cells were seen in this plexus.

The sympathetic (hypogastric) plexus along the aorta and common iliac arteries, showed to the naked eye numerous spindle-shaped thickenings, even on the most minute nerve filaments, which were thus easily identified, running along the iliac vessels and in the mesentery.

The sympathetic plexus in the subserous coat of the stomach was also very evident through the peritoneum, in virtue of the spindle-shaped thickenings of the individual nerve filaments, especially along the lesser curvature and running towards the pylorus.

The left cervical sympathetic cord; the main cord itself between the ganglia was very little thickened, but the minute communicating filaments showed spindle-shaped thickenings. In the situation of the middle cervical ganglion, which measured 8 mm. in diameter, the increase in thickness appeared to be due to fibromatosis of the bundles of medullated nerve fibres passing through it and leaving it. The change was the same as that observed in the cerebro-spinal nerves. The ganglion cells, though here and there more or less surrounded and displaced by the fibromatosis, did not appear to have suffered.

6. *Multiple neuro-fibromata in the nerve trunks, and in the nerve roots within the spinal canal, causing wide-spread paralysis; spontaneous and incomplete recovery from the paralysis; death from pneumonia.*

A. M., forty-one, wool-spinner, Jedburgh, admitted to the Longmore Hospital 19th June 1894. He belongs to a very healthy family, and has three children of his own. The only illness he has had since childhood was an attack of erysipelas at the age of eighteen. He has always been very temperate with alcohol. During the last six years he has suffered from repeated boils on the palmar surface of the right forearm. Four years ago he accidentally noticed a lump in his left upper arm; this was removed by Professor Annandale in the Royal Infirmary; there is no record of this tumour. The scar is parallel with and behind the line of the brachial artery in the upper half of the left upper arm, apparently in the line of the ulnar

nerve. He states that after the operation there was a feeling of "pins and needles" down the arm, that the hand was weak and stiff, and that he moved the fingers with difficulty. The disability of the arm improved sufficiently to allow of his resuming work.

A few months later (*i.e.* about three and a half years ago) he began to suffer from a dull heavy pain in the back, and of "pins and needles" sensations, and of occasional twitchings in the right foot; then the foot began to drag on walking, and he had to use a stick in going to and from his work; the great toe often caught in the ground and tripped him. After stooping he had great difficulty in straightening himself again. A dull pain also developed in his left knee, with a feeling of "pins and needles" about the joint. He continued his work under difficulties until two years ago, when, in addition to his other troubles, the right arm became affected with weakness and with the sensation of "pins and needles"; he could no longer guide things properly at his work, and it required an effort to move the elbow and wrist. A year ago he was admitted to the University Clinical Wards, Royal Infirmary, Edinburgh, under the care of Professor Fraser and Dr Bruce, to whom I am indebted for the following notes as to his condition at that time.

He is fairly nourished; there is no undue pigmentation of the skin; there are scars of previous boils on the right forearm. He is of average intelligence. He sleeps well at night. The following tumours were recognised:—

Two subcutaneous pea-like nodules over the lower end of the sternum.

A large tumour, the size of an orange, towards the apex of the right axillary space; when it is compressed a slow contraction of the pectoralis major takes place.

A small tumour in the substance of the right ulnar nerve, one inch above the elbow.

A small tumour on the inner aspect of the left upper arm at the outlet of the axilla.

Three small tumours in the right supra-clavicular triangle.

Three tumours of considerable size in the back of the right thigh between the tuber ischii and the knee joint; on compressing any one of these, the limb is drawn up involuntarily; the thigh being flexed on the abdomen, the leg on the thigh, and the foot on the leg (dorsal flexion of the foot).

A tumour the size of a cherry on the anterior aspect of the right leg midway between the knee and ankle.

The largest tumour (11 × 11 cm.) is situated in the position of the left obturator nerve in the inner part of Scarpa's triangle, immediately below Poupart's ligament, displacing the femoral vessels outwards, and the adductor muscles inwards; when the tumour is compressed, the limb is forcibly and involuntarily adducted. Although the majority of the above tumours are sensitive, they are not markedly painful on pressure. None of them are the seat of spontaneous pain.

Motor and sensory functions.—He complains of numbness in the right leg, foot, hand, and left knee. In walking he drags one foot after the other; the right foot drags most. There are fibrillary tremors in the deltoid, biceps and triceps of both arms, and undulating tremors in the calf and anterior tibial muscles. There are occasional painful cramps in both legs during which the legs are drawn up involuntarily; they occur frequently both day and night; he is unable to extend the legs after they are drawn up. The legs are fairly muscular; the muscles of the right calf are, however, smaller and softer that those of the left. The organic reflexes are normal. The knee-jerks are present. There is no ankle clonus. Co-ordination is defective in all four extremities; he cannot describe circles properly with either foot; when standing with the eyes shut he tends to stagger and fall. The tactile sensibility is fairly good,

but the localising power is defective. Sensibility to pain is a little blunted and erratic. Sensibility to heat is a little blunted and delayed. The pupils and fundus of the eyes are normal.

Clinical history continued.—For four months he was able to walk about the ward; he then became unable to stand, and he was confined to bed altogether; his arms became so powerless that he let anything fall which he tried to grasp, and he had to be fed. A little later he ceased to be able to raise himself in bed from the recumbent to the sitting posture, nor could he maintain his position when lifted up; he appeared to have lost power in his abdominal muscles. He could not turn in bed. When put into a wheel chair, he had to be firmly secured with a sheet to prevent him falling forwards, or to one or other side. At this stage tactile sensibility varied very much; sometimes it was quite normal, at other times it was very uncertain. He complained of creepy sensations round the shoulders and root of the neck, and of constriction round the belly at the level of the navel. The knee-jerks became exaggerated. He never had a catheter passed; the urine used to come away of itself and dribble for a few days from time to time, then for perhaps three weeks the bladder functions would be normal. The bowels moved without his control when the motions were liquid after medicine. During this period of helplessness he had very little pain apart from the occasional cramps in the legs; he took his food and slept well.

He was treated with iodide of potassium and thyroid extract; nothing appeared to have any influence on his troubles except the battery, after which he was able to move his legs about the bed more easily.

He was transferred to the Longmore Hospital on 19th June 1894, and remained there until he died of an intercurrent pneumonia four and a half years later (3rd January 1899). After about nine months' residence in the Longmore Hospital, he gradually recovered

power in the arms, and was again able to feed himself; three months later, he was able to sit up in bed when propped up with pillows; there was least improvement in the legs, although he fancied he could move them about more easily in bed. As time went on he was able to sit up unassisted in a common wheel chair for two or three hours at a time. He had only one attack of dribbling of urine after admission, and the bowels never moved without his control. He must always lie on a water-bed; he was once without one for a fortnight, and a bed-sore threatened over the sacrum. His general health is excellent; there is a tendency to clubbing of the nails. The feet are in an attitude of slight equino-varus; the lesser toes are drawn up like claws; the muscles of the legs are considerably wasted; both knee-jerks are exaggerated, and there is ankle clonus on the left side. He can lift both legs off the bed; he can flex them at the knee and hip, and can abduct at the hip. Movements of the foot and toes are limited to increasing the attitude of equino-varus. The sensory functions are quite normal. The tumours do not appear to have changed in any way since they were first recorded, except that the pea-like tumours over the lower end of the sternum have disappeared. On squeezing those situated in the motor nerve trunks, there are spasmodic jerkings of the muscles supplied by the nerves involved. The accessible nerve trunks in both upper arms are easily palpated, and appear to be irregularly thickened. There is a slight degree of right total scoliosis. The trunk muscles are wasted. The great pectorals are much reduced in size.

I saw him last on the 6th October 1898, two months before his death. His general condition was the same as before. There was no complete paralysis of any muscle or group of muscles, although the movements of the limbs were decidedly feeble and clumsy. The knee-jerks, which were formerly exaggerated, now responded very feebly. There was irregular clonus at the left ankle. The plantar reflexes were exaggerated. His death (from intercurrent pneumonia)

was quite unexpected. There was no opportunity of making a post-mortem examination.

Remarks on the preceding case.—This case exhibits features which are exceptional in generalised neuro-fibromatosis, viz. : the pronounced disturbances of motion (cramps, inco-ordination, paralysis) and of sensation (numbness, pins and needles, girdle-sensation) ; the alterations in the reflexes (exaggeration of the knee-jerks and of the plantar reflexes, presence of ankle clonus) ; the tendency to bed-sores ; and the partial and occasional paralysis of the bladder and rectum. The wide distribution of these phenomena over the trunk as well as all four limbs ; the irregularity or inequality of the distribution in the different limbs and segments of limbs would appear to indicate that the phenomena were the result of multiple tumours of the nerve roots scattered up and down within the spinal canal, causing pressure upon the nerve roots, and upon the cord itself (compression-myelitis). The variations in the degree and extent of the nerve lesions during the five years the patient was under observation, and especially the remarkable recovery from motor paralysis of several months' duration, exhibited more particularly in the upper extremities, would appear to be more in harmony with the diagnosis given than with any other. It is to be borne in mind that the lesion which we call neuro-fibromatosis, or multiple tumours of nerves, is capable of considerable modification, in the sense that the so-called tumours may vary very much in size from time to time ; they may increase or diminish in size with considerable rapidity from causes which are as yet unknown, but which may be attributed to variations in their vascularity and to the amount of fluid in the overgrown endoneurium of which the tumours are composed. The notes of the case bring out the interesting fact also, that two of the small subcutaneous tumours (over the lower end of the sternum) actually disappeared during the same period as that in which the subsidence of the paralytic phenomena took place.

Elephantiasis neuromatosa of the right lower extremity dating from puberty; amputation of thigh; permanent recovery.[1]

Mrs G., twenty-eight, admitted to the University Clinical Wards, Royal Infirmary, Edinburgh, 28th May 1894, under the care of Professor Annandale. Her family history was good, and she had never resided out of Scotland. Her first and only illness consisted in an attack of what was called erysipelas in the right leg, at the age of twelve. She made a good recovery from this, but a year later her father noticed that the right leg was thicker than the other; it caused her no inconvenience, but it gradually increased, and she was obliged to wear a larger shoe and stocking. The increase in size of the leg continued, and although she was never laid up with it, and was able to begin work in a mill, she found that the weight and bulk of the limb impeded her movements. In 1889, at the age of twenty-three, Professor Annandale removed a large pendulous mass of skin and cellular tissue from the back of the thigh. Shortly after this she married and gave birth to two healthy children, the second of which she nursed herself. She was quite convinced that the increase in the size of the limb had been more rapid since her marriage. Although it never gave her any pain, it has become quite a burden to her. She is a muscular, healthy looking woman, perfectly normal in every respect, apart from the right lower extremity (Plate XVI.). The enlargement of the limb extends from the junction of the upper and middle thirds of the thigh to the toes. In the foot, from the malleoli downwards, there is comparatively little swelling. In the leg the swelling is enormous, and projects chiefly on the posterior and inner aspects, and overhangs the foot. In the thigh the swelling is more localised to the posterior aspect, and gradually tapers off into the normal contour of the limb above. The measurements of the circumference of the two limbs are as follows:—

[1] This case has been reported by Professor Annandale in the third volume of the Edinburgh Hospital Reports.

	Right.	*Left.*
Middle of thigh .	70 cm.	35·5 cm.
Knee . . .	48·5 „	29 „
Middle of calf .	71·2 „	25·3 „
Middle of foot .	26·7 „	22 „

The skin of the affected area is coarse, uneven, and hard in consistence; in parts it resembles morocco leather, in other parts it is like the hobnailed surface of a cirrhotic liver; it is unbroken throughout, is quite dry, and devoid of any hairs or visible pigmentation. There are two localised thickenings of the epidermis resembling warts. At the lower and posterior part of the thigh there are pendulous masses or tumours, separated from each other by deep folds or fissures; most of these projecting masses are firm and hard, some of them are soft, flabby, and semi-fluid. There is no œdema and the skin does not pit on pressure.

The sensibility of the skin is, on the whole, diminished; she occasionally complains of pricking sensations.

The motor functions are normal, except in so far as the movements are interfered with by the bulk of the swelling. The accessible nerve trunks appear to be normal.

The diagnosis arrived at was elephantiasis neuromatosa.

As regards treatment, the question was considered of flaying the limb of the affected skin and subcutaneous tissues in instalments, with subsequent Thiersch grafting; Professor Annandale decided in favour of amputation. This he did through the upper third of the thigh on 6th June 1894. The limb was first suspended, so as to empty it of blood; an elastic tourniquet was applied at the root of the limb; the limb was rapidly removed by equal transfixion flaps. The wound healed rapidly, and she left the hospital very satisfied with the improvement in her condition. She has remained well ever since, and has given birth to another

child. The limb is preserved in the Anatomical Museum of the University of Edinburgh. The muscles throughout are of normal colour and development; the cortex of the femur is unusually thick and dense; the main vessels and nerves were examined microscopically and found normal; the lesion appeared to be confined to the subcutaneous cellular tissue and skin, and to consist in the formation of a watery, glistening, greyish-white tissue, between the epidermis on the surface and the subjacent fascia lata and muscles of the limb. This new tissue replaced the normal cutaneous and subcutaneous fat; at the level of the amputation it was observed mixed with or infiltrating the fat, the latter being about one inch in depth; lower down the limb the fat had entirely disappeared from the subcutaneous tissue. The newly-formed gelatinous tissue exuded an abundant watery fluid. In parts it was whiter, drier, and firmer in consistence, showing an areolar arrangement of white fibrous bundles, with a softer and more gelatinous tissue in its meshes. The proportion of the firm fibrous tissue and of the semi-fluid gelatinous tissue varied in different parts of the limb. The localised tumour-like elevations or masses on the posterior aspect were composed of the same new tissue, and exhibited also similar variations in the proportions of the firm and softer varieties.

Microscopical examination.—The epidermis, apart from a little increase in the amount of pigment in the deeper layers of the rete Malpighii, is not altered. The pars papillaris of the true skin is only altered in so far as many of the papillæ are flattened out, and the normal regular arrangement of the papillæ is lost. The pars reticularis is the seat of a diffuse overgrowth of connective tissue; there is no hard and fast line, however, bounding it from the papillary layer towards the surface and the subcutaneous connective tissue beneath. The newly-formed connective tissue, which entirely replaces the normal fat of the corium, is, for the most part, fibrous in character, the fibrous bundles being generally closely

arranged in a plexiform manner, and being very deficient in cells.

Scattered throughout this fibrous tissue are the sweat glands and their ducts, the hair follicles and their associated muscles, a very limited number of sebaceous glands, certain cellular areas, which under a low power look not unlike miliary tuberculous granulations, and thickened nerve filaments. The sweat glands generally have undergone no structural alteration; they are, however, much displaced, many of them are deeply situated so that they are in immediate relation to the subcutaneous tissue, and the ducts belonging to them are much elongated, and to a large extent, straightened out or uncoiled. There is an entire absence of any special formation of new fibrous tissue surrounding the sweat glands, as is usually observed in such cases; if anything, the appearance is rather that of glands surrounded by scanty remains of the original tissue of the cutis containing fat cells. The hair follicles and sebaceous glands are unaltered except that one or two of the latter appear to have become distended into cysts.

The cellular areas already referred to, are all related to, and for the most part surround, the thickened terminal nerve filaments in the altered pars reticularis of the corium; these cellular areas are scattered irregularly throughout the fibrous meshwork of the pars reticularis, some of them are rounded or oval, others are more elongated and branching, and of these latter, some are prolonged into the papillary portion; they contrast very definitely with the more fibrous tissue in which they are embedded, by their more cellular character, being packed with nuclei, both round and spindle-shaped. Being systematically related to nerve fibres, either solitary or collected into bundles, they may be reasonably assumed to originate in connection with these. Nerve bundles when cut in longitudinal section show multiplication of the nuclei between the individual fibres; when a solitary nerve fibre is cut longitudinally

the nuclei surrounding it are directly continuous with those of the cellular areas in relation to the nerve filaments.

The blood-vessels of the skin show no visible alteration.

The subcutaneous tissue retains very little of its normal characters; the fat lobules are split up and separated by a tissue which consists of a wide-meshed, finely fibrillated reticulum, the spaces of which are either empty (and therefore were probably occupied by fluid), or contain a few leucocytes, branching connective tissue corpuscles and granules of precipitated mucin. Running through this altered subcutaneous tissue from below, towards the skin, are connective tissue processes or septa containing the larger blood-vessels and bundles of nerve fibres; the latter again present the multiplication of the endoneurial nuclei described in the nerve bundles of the cutis vera. When a nerve bundle splits up into its terminal isolated fibres, these are thickly surrounded by proliferated young connective tissue corpuscles (derived from the endoneurium?) these being here and there collected into rounded masses. Unless the sections had been stained according to Weigert's method, it would not have been possible to have observed the relationship between the newly-formed tissue and the nerves.

CHAPTER VIII

THE TRAUMATIC OR "STUMP NEUROMATA"

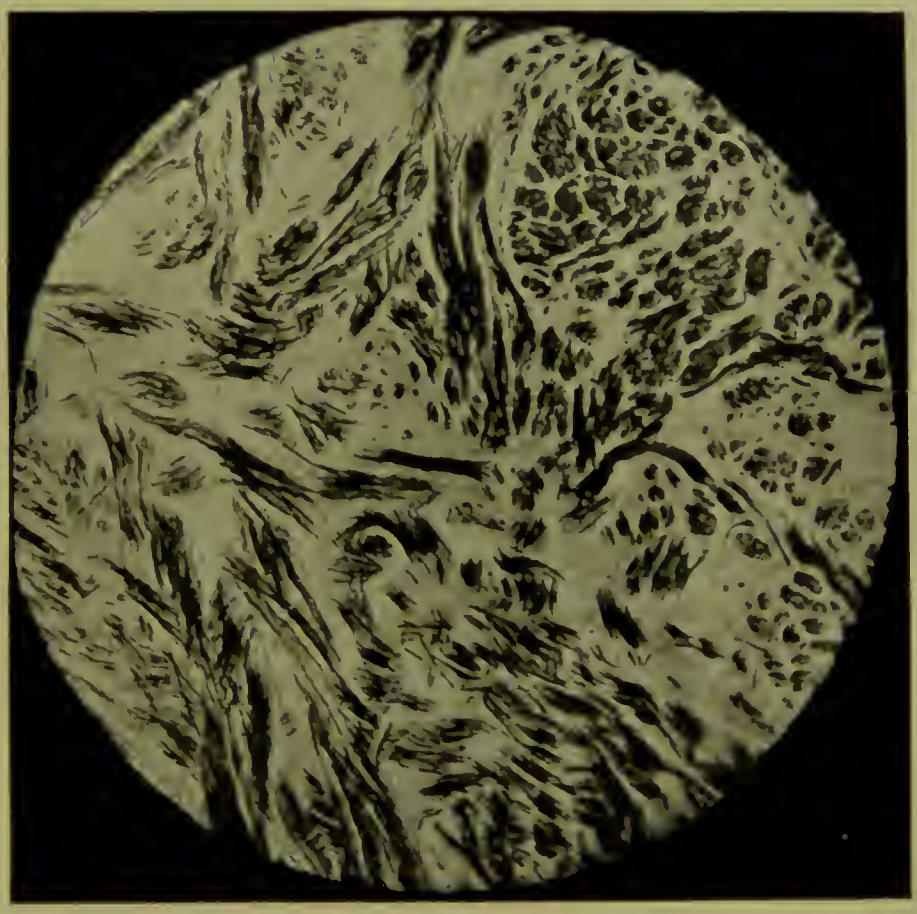
Although the "stump neuromata" are only tumours in the clinical sense, they are regarded as being closely allied to the true neuromata, because they have been shown to possess nerve fibres of new formation.

They may follow upon any gross injury of a nerve, *e.g.* when it is divided (hence the term "division neuromata") or torn across or ligatured. Their formation is related to the reparative changes which ensue when a nerve has been injured, and which, within certain limits, are to be regarded as a more or less constant accompaniment of the process of repair. It has long been known that when a stump is examined some months after an amputation, the cut ends of the nerves are enlarged and present the appearance of bulbs. It is also well-known that when a nerve is divided in its continuity both ends may present a bulbous enlargement, that at the central end being the larger of the two. There are exceptional cases on record in which a nerve has been partially severed or torn across (*e.g.* in punctured wounds), or in which a foreign body has lodged in its substance, and a localised enlargement of the nerve has taken place; the best known example is that described by Dr Denmark, in which a portion of a bullet lodged in the musculo-spiral nerve; the enlargement of the nerve disappeared when the foreign body was removed.

It would appear, therefore, that the formation of a moderate bulbous swelling at the cut end of a nerve, is to be regarded as a normal or physiological process, analogous to the formation of callus in the repair of injuries of bone; in certain circumstances the process

may be exaggerated, and result in the formation of larger bulbs or tumours which may be regarded as abnormal or pathological, and which are analogous to the excessive formation of callus in injuries of bone. It is necessary that we should briefly consider the nature of the changes when a nerve trunk is divided in its continuity in cases in which the wound pursues an aseptic course. The bulbous enlargement which forms in relation to either end of the nerve, was at first supposed to consist of scar tissue (hence the name "cicatricial neuromata"); microscopic examination has shown, however, that the most constant and important constitnent of the bulb is a dense plexus of young nerve fibres. This has been demonstrated not only in the bulb at the central end, but also in that at the distal extremity. Without recapitulating the various views that have been advanced as to the nature and origin of the young nerve fibres, we may accept those submitted by Robert Kennedy to the Royal Society of London in 1897, as having found most favour both with physiologists and with clinicians. Kennedy holds that the young nerve fibres are not mere prolongations of the old axis cylinders, which had been cut across, but are of new formation from the cells belonging to the sheath of Schwann. The old axis cylinders undergo degeneration, both in the distal end and in the terminal portion of the central end. The young or newly formed nerve fibres are able to attain maturity in the case of the proximal end, probably because it is in continuity with the nerve centre; those in the peripheral end remain in an immature condition until their continuity with the nerve centre has been restored by operation and suture. These observations are in harmony with the clinical fact, that nerve conduction may be rapidly re-established after such operations, the young nerve fibres in the distal end being ready to take on this function; this refers especially to the sensory functions; the recovery of the motor functions may be long delayed, or may never take place at all, on account of the secondary changes which occur in the muscles,

PLATE XIX.



Section of a stump neuroma, showing bundles of young nerve fibres running in all directions.

Weigert. *Leitz No. 3 objective.*

which may have progressed beyond recovery. Kennedy's observations are in harmony with the appearances observed in the normal bulbous swellings at the cut ends of nerves ; viz., an enormous number of young nerve fibres arranged in a dense plexus (Plate XIX.). In sections of bulbs, the nerve fibres are seen running in all directions, some of them on reaching the extremity of the bulb run backwards towards the nerve trunk from which they are derived. The nerve fibres are embedded in newly-formed connective tissue which varies very much in amount, and which varies in structure from granulation tissue to fully-developed fibrous tissue, according to the time which has elapsed since the nerve was cut across. The direction of growth assumed by the young nerve fibres is not so much influenced by purely mechanical conditions, as by an alleged chemical attraction exerted by nerve tissue ; Forsmann has shown by a series of interesting experiments on rabbits and guinea pigs, that the peripheral end of a divided nerve seemed to exert a decided attraction (which he calls positive neuro-tropismus) on the direction of growth of the young nerve fibres growing out from the central end of the nerve. This may probably explain the observation alluded to above, that in the stump neuroma, in which there is no peripheral end to attract the young nerve fibres, they turn backwards, or double on themselves, in the direction of the nerve trunk from which they are derived. The abnormally large bulbs (stump neuromata) which are occasionally met with, are to be regarded as pathological, and as the result of some external factor interfering with the normal process of repair ; the external factors concerned are probably those which excite the formation of granulation tissue and of scar tissue, and are similar to those which are known to excite the excessive formation of bone in injuries and diseases of the skeleton. One of the most important influences would appear to be the occurrence of bacterial infection and inflammation ; certain it is that stump-

neuromata of the large and troublesome kind have become rarer and rarer as the principles of Listerian surgery have been more successfully carried out. In cases in which the bacterial infection has been unusually severe, the nerve fibres may undergo complete destruction, and the cut ends of the nerve may be atrophied and wasted instead of presenting bulbous enlargements. There are probably other factors, *e.g.* pressure, presence of a foreign body, etc., which may influence the amount of connective tissue which is formed, and affect, therefore, the size of the bulbs at the ends of the nerves, since in the same stump different nerves may present varying degrees of enlargement, and there may be a want of proportion between the size of the nerve and the size of the bulb at its extremity.

The general appearances of the stump-neuroma are illustrated in Plate XX. They vary considerably in size and shape; they may present a capsule of smooth shining exterior, like that of a normal nerve trunk, or they may be more or less incorporated with the scar tissue; where there are several nerves in a stump, they may be fused together into a common mass, or the individual bulbs may be connected to each other by strands of scar tissue. The occasional presence of a bulb above the cut end of a nerve is probably to be attributed to its having been accidentally injured at that point in the process of amputation, and having been then completely cut across, at a lower level.

The clinical features of stump-neuromata are a little difficult to define, because many of the symptoms for which they are blamed may arise from other causes. It is certain that neuromata of considerable size may be present in a stump for years without giving rise to any symptoms, and that there are many cases in which the symptoms characteristic of neuroma have been found to be due to a neuritis, to the involvement of the end of a nerve in the scar tissue, to a nerve being pressed upon over the end of a bone, or its inclusion

PLATE XX.



Stump neuromata of the sciatic nerve.
(Excised by Mr A. G. Miller, forty years after the original amputation through the thigh.)
Natural size.

in the ligature of an artery, etc. Symptoms suggesting neuromata are more common in the lower limb, partly because of the use of a badly-fitting artificial support, and partly also because more legs are amputated than arms. There is more likely to be suffering in those in which the wound has suppurated. The period of onset of symptoms varies within very wide limits, from a few months to twenty or more years after the amputation.

The tumours may be recognised by palpation when they are large enough, and are superficially situated. It is possible to feel them in the sciatic nerve in the thigh. They may cause no symptoms or they may be very sensitive and the source also of spontaneous pains. The pain may be limited to the stump and shoot down to the scar, or it may shoot up the limb towards the trunk ; sometimes it shoots down to a part which no longer exists. It is occasionally described as "burning" or "electric," and it is said to vary with changes in the weather, with circulatory disturbances, etc., as in other neuroses. Muscular spasms, twitchings of the stump, tremblings and even epileptiform seizures have been described, but it is doubtful if these are to be attributed to the neuroma, although cases are recorded by older authors in which the removal of a stump-neuroma has been followed by disappearance of the epileptiform attacks.

The clinical features of the bulbous enlargements which develope when a nerve is divided in its continuity, are of a similar character to those described in stumps, with the addition of the loss of function resulting from the nerve having been divided.

The treatment may be considered from the point of view of prevention ; in amputating a limb the nerve trunks are to be drawn out and cut off with the scissors as high as possible ; care is to be taken not to include a nerve trunk in any of the ligatures of the blood-vessels.

When stump-neuromata are believed or known to exist, and are

giving rise to symptoms, operative interference may take the form of nerve stretching, excision of the tumours along with a portion of the nerves involved, or reamputation. Inasmuch as the first of these may be, and often has been, attended with relapse of the symptoms, and that the third (reamputation) is usually unnecessary, the procedure of choice is to expose the affected nerve trunk as well as its terminal bulb, and to excise them, removing as much of the nerve trunk as will ensure immunity from trouble in the future.

The operative treatment of the bulbs which form in relation to nerves divided in their continuity, belongs to the treatment of divided nerves, and is beyond the scope of the present work.

Personally observed Case of Stump-Neuromata

1. *Neuromata in stump, forty years after amputation of thigh, causing pains shooting down to the toes; stretching of sciatic nerve; relief for twelve months; relapse of symptoms; excision of tumours along with a portion of the nerve; recovery.*

A. F., sixty-five, gas-stoker, Leith, married, was admitted to the Royal Infirmary, under the care of Mr A. G. Miller, 24th October 1896. The patient stated that he had suffered amputation through the lower third of the left thigh, for injury, about forty years ago. About twenty years ago he began to complain of shooting pains in the stump; these continued to trouble him from time to time until five years ago, when the sciatic nerve was stretched in the upper third of the thigh by Mr Miller; the pains disappeared for twelve months, then returned, and have continued up till now, becoming gradually worse. He has had recourse to morphine both by the mouth and by hypodermic injection. On admission he was found to be a robust man for his years. He complained of hot shooting pains in the stump

of the left thigh running down to the toes which are worse in damp weather and at night, when they interfere with sleep.

The original amputation wound appears to have suppurated, since there is a considerable amount of scar tissue, and adhesion of the cutaneous scar to the deeper tissues and to the bone. On the posterior aspect of the thigh, and a little above the scar, there are two egg-shaped tumours lying side by side, about the size of olives, slightly sensitive on pressure, and allowing of some lateral movement. Mr Miller cut down on these on the 30th October 1896, and removed them along with a portion of the sciatic nerve. The larger tumour (Plate XX.) measured 3·5 cm. in length, 3·5 in breadth, and 2 in thickness. The sciatic nerve, where divided, measured 12 × 10 mm. and tapered down to 9 × 5 mm. immediately above the larger tumour. About 2 cm. above the latter, it gave off a branch, 4 mm. in diameter, which terminated in a smaller bulbous tumour. This smaller tumour was, at one point, firmly adherent to the scar tissue, otherwise, the tumours as well as the trunk of the nerve, had a smooth polished exterior, from which the investing tissues were easily peeled off.

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